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L6 ANSWER 9 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:617981 CAPLUS
DOCUMENT NUMBER: 127:253211
TITLE: Method of promoting bone growth with hyaluronic acid and growth factors
INVENTOR(S): Radomsky, Michael
PATENT ASSIGNEE(S): Orquest, Inc., USA
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9732591	A1	19970912	WO 1997-US4810	19970305
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, YU				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2246747	AA	19970912	CA 1997-2246747	19970305
AU 9725449	A1	19970922	AU 1997-25449	19970305
AU 729086	B2	20010125		
CN 1212628	A	19990331	CN 1997-192822	19970305
EP 910389	A1	19990428	EP 1997-916976	19970305
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
NZ 331238	A	20000526	NZ 1997-331238	19970305
JP 2002504083	T2	20020205	JP 1997-532070	19970305

PRIORITY APPLN. INFO.:

US 1996-611690	A	19960305
US 1997-811971	A	19970305
WO 1997-US4810	W	19970305

AB A bone growth-promoting composition is provided comprising hyaluronic acid and a growth factor. The composition has a viscosity and biodegradability sufficient to persist at the site of desired bone growth for a period of time sufficient to promote the bone growth. Preferably hyaluronic acid is used in a composition range of 0.1 to 4 % and preferred growth factor is bFGF, present in a concentration range of 10-6 to 100 mg/mL. An aqueous solution containing Na hyaluronate, bFGF, and Na citrate was injected with a needle between the periosteum and parietal bone of rats. The animals were euthanized 14 days following treatment and new bone formation was evaluated.

L18 ANSWER 31 OF 87 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:294955 CAPLUS
DOCUMENT NUMBER: 134:290753
TITLE: Method of promoting bone growth with hyaluronic acid and growth factors
INVENTOR(S): Radomsky, Michael
PATENT ASSIGNEE(S): Orquest, Inc., USA
SOURCE: U.S., 11 pp., Cont.-in-part of U.S. 5,942,499.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6221854	B1	20010424	US 1999-360543	19990726
US 5942499	A	19990824	US 1997-811971	19970305
CA 2378328	AA	20010201	CA 2000-2378328	20000726
WO 2001007056	A1	20010201	WO 2000-US20373	20000726
WO 2001007056	C2	20020725		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1198235	A1	20020424	EP 2000-950736	20000726
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003505422	T2	20030212	JP 2001-511940	20000726
NZ 516097	A	20040227	NZ 2000-516097	20000726
AU 777328	B2	20041014	AU 2000-63797	20000726
US 2001014664	A1	20010816	US 2001-825688	20010403
US 6703377	B2	20040309		
US 2004176295	A1	20040909	US 2004-796441	20040308
AU 2005200146	A1	20050210	AU 2005-200146	20050113

PRIORITY APPLN. INFO.:		
US 1996-611690	B2	19960305
US 1997-811971	A2	19970305
US 1999-360543	A	19990726
WO 2000-US20373	W	20000726
US 2001-825688	A1	20010403

AB A bone growth-promoting composition is provided comprising hyaluronic acid and a growth factor. The composition has a viscosity and biodegradability sufficient to persist at an intra-articular site of desired bone growth for a period of time sufficient to promote the bone growth. Preferably hyaluronic acid is used in a composition range of 0.1-4% by weight and preferred growth factor is bFGF, present in a concentration range of about 10#-6 to 100 mg/mL.

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 19 OF 23 MEDLINE on STN
ACCESSION NUMBER: 1999116173 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9917648
TITLE: Potential role of fibroblast growth factor in enhancement of fracture healing.
AUTHOR: Radomsky M L; Thompson A Y; Spiro R C; Poser J W
CORPORATE SOURCE: Orquest Inc., Mountain View, CA 94043-5712, USA.
SOURCE: Clinical orthopaedics and related research, (1998 Oct) No. 355 Suppl, pp. S283-93.
Journal code: 0075674. ISSN: 0009-921X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199902
ENTRY DATE: Entered STN: 23 Feb 1999
Last Updated on STN: 3 Mar 2000
Entered Medline: 10 Feb 1999

AB Fibroblast growth factors are present in significant amounts in bone and several studies have suggested that they may be involved in normal fracture healing. It is well established that fibroblast growth factors have mitogenic and angiogenic activity on mesoderm and neuroectoderm derived cells. Of particular interest as a member of the fibroblast growth factor family, basic fibroblast growth factor stimulates mitogenesis, chemotaxis, differentiation, and angiogenesis. It also plays an important role in the development of vascular, nervous, and skeletal systems, promotes the maintenance and survival of certain tissues, and stimulates wound healing and tissue repair. Animal studies have shown that the direct injection of fibroblast growth factor into fresh fractures stimulates callus formation, which provides mechanical stability to the fracture, accelerates healing, and restores competence. The matrix used to present the fibroblast growth factor at the fracture site plays a critical role in the effectiveness of the treatment. The evaluation of injectable basic fibroblast growth factor in a sodium hyaluronate gel for its effectiveness in stimulating fracture healing is described. When applied directly into a freshly created fracture in the rabbit fibula, a single injection of the basic fibroblast growth factor and hyaluronan results in the stimulation of callus formation, increased bone formation, and earlier restoration of mechanical strength at the fracture site. The hyaluronan gel serves as a reservoir that sequesters the basic fibroblast growth factor at the injection site for the length of time necessary to create an environment conducive to fracture healing. It is concluded that basic fibroblast growth factor and sodium hyaluronate act synergistically to accelerate fracture healing and that the combination is suitable for clinical evaluation as a therapy in fracture treatment.

L1 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:332901 CAPLUS
DOCUMENT NUMBER: 125:19048
TITLE: Fibroblast growth factors for the treatment of eye diseases
INVENTOR(S): Belkin, Michael; Savion, Naphtali; Landshman, Nahum
PATENT ASSIGNEE(S): Ramot University for Applied Research and Industrial Development Ltd., Israel
SOURCE: U.S., 9 pp., Cont. of U.S. Ser. 673, 867, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5510329	A	19960423	US 1992-997664	19921228
PRIORITY APPLN. INFO.:			US 1992-997664 B1	19921228
			US 1991-673867 B1	19910322
			US 1988-185893	19880426

AB The invention relates to compns. which induce regeneration of the corneal endothelium. The compns. are of value in regenerating the corneal endothelium in humans, which is frequently damaged in the course of eye surgery and injuries. Such regeneration is very important to ensure the full functionality of the eye. The compns. comprise as active ingredient an adequate quantity of fibroblast growth factor in a suitable physiol. acceptable vehicle. A preferred embodiment of the invention relates to a composition containing a certain quantity of hyaluronic acid and any other viscoelastic agent.

L1 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:480271 CAPLUS
DOCUMENT NUMBER: 119:80271
TITLE: Compositions containing fibroblast growth factor for treatment of the eyes
PATENT ASSIGNEE(S): Ramot University Authority for Applied Research and Industrial Development Ltd., Israel
SOURCE: Israeli, 16 pp.
CODEN: ISXXAQ
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
IL 82295	A1	19930221	IL 1987-82295	19870422
PRIORITY APPLN. INFO.:			IL 1987-82295	19870422

AB An ophthalmic preparation for enhancing regeneration of the corneal endothelium before and during surgery of the eye, for improving donor endothelium preservation prior to keratoplasty, and for use in cases of injury and disease, comprises fibroblast growth factor and a viscosity enhancer selected from hyaluronic acid, its salts, chondroitin sulfate, Me cellulose, and water-soluble collagens.

L1 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:617981 CAPLUS
DOCUMENT NUMBER: 127:253211
TITLE: Method of promoting bone growth with hyaluronic acid and growth factors
INVENTOR(S): Radomsky, Michael
PATENT ASSIGNEE(S): Orquest, Inc., USA
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9732591	A1	19970912	WO 1997-US4810	19970305
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, YU				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2246747	AA	19970912	CA 1997-2246747	19970305
AU 9725449	A1	19970922	AU 1997-25449	19970305
AU 729086	B2	20010125		
CN 1212628	A	19990331	CN 1997-192822	19970305
EP 910389	A1	19990428	EP 1997-916976	19970305
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
NZ 331238	A	20000526	NZ 1997-331238	19970305
JP 2002504083	T2	20020205	JP 1997-532070	19970305

PRIORITY APPLN. INFO.:

US 1996-611690	A	19960305
US 1997-811971	A	19970305
WO 1997-US4810	W	19970305

AB A bone growth-promoting composition is provided comprising hyaluronic acid and a growth factor. The composition has a viscosity and biodegradability sufficient to persist at the site of desired bone growth for a period of time sufficient to promote the bone growth. Preferably hyaluronic acid is used in a composition range of 0.1 to 4 % and preferred growth factor is bFGF, present in a concentration range of 10-6 to 100 mg/mL. An aqueous solution containing Na hyaluronate, bFGF, and Na citrate was injected with a needle between the periosteum and parietal bone of rats. The animals were euthanized 14 days following treatment and new bone formation was evaluated.

L10 ANSWER 12 OF 12 MEDLINE on STN
ACCESSION NUMBER: 96212618 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8629452
TITLE: Basic fibroblast growth factor for stimulation of bone formation in osteoinductive or conductive implants.
AUTHOR: Wang J S
CORPORATE SOURCE: Department of Orthopedics, University of Lund, Sweden.
SOURCE: Acta orthopaedica Scandinavica. Supplementum, (1996 Apr) Vol. 269, pp. 1-33. Ref: 204
Journal code: 0370353. ISSN: 0300-8827.
PUB. COUNTRY: Denmark
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199606
ENTRY DATE: Entered STN: 8 Jul 1996
Last Updated on STN: 8 Jul 1996
Entered Medline: 21 Jun 1996

AB Basic Fibroblast Growth Factor (bFGF) is one of the endogenous factors found in bone matrix. bFGF is a mitogen for many cell types, including osteoblasts and chondrocytes. It can stimulate angiogenesis and osteoblast gene expression. The purpose of this study was to investigate whether exogenous bFGF can stimulate the formation of bone in bone grafts and in a bone graft substitute. In a model using demineralized bone matrix implants for bone induction, a dose of 15 ng bFGF per implant increased the number of chondrocytes and the amount of bone, whereas 1900 ng greatly inhibited cartilage and bone formation. These results are consistent with previous studies with this model, showing that a lower dose of bFGF increased bone calcium content and a higher dose reduced it. Thus, exogenous bFGF can stimulate proliferation during early phases of bone induction. A new device, the bone conduction chamber, was developed for the application of bFGF to bone conductive materials. This model made it possible to demonstrate a difference between the conductive properties of bone grafts and porous hydroxyapatite. bFGF increased bone ingrowth into bone graft inside the chamber and showed a biphasic dose-response curve, so that 8-200 ng per implant (0.4-10 ng/mm3) increased bone ingrowth, but higher or lower doses had no effect. The same doses had the same effects in porous hydroxyapatite. In both bone grafts and porous hydroxyapatite, the highest dose still caused an increase in ingrowth of fibrous tissue. The effect on bone ingrowth was first detected after 6 weeks, regardless if administration of bFGF started at implantation or 2 weeks later, using an implanted minipump. Hyaluronate gel was effective as a slow-release carrier for bFGF. In conclusion, bFGF stimulates bone formation in bone implants, depending on dose and method for administration.

L1 ANSWER 10 OF 10 MEDLINE on STN
ACCESSION NUMBER: 2003369126 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12903682
TITLE: Effect of growth factors on hyaluronan production by canine vocal fold fibroblasts.
AUTHOR: Hirano Shigeru; Bless Diane M; Heisey Dennis; Ford Charles N
CORPORATE SOURCE: Department of Surgery, Division of Otolaryngology-Head and Neck Surgery, University of Wisconsin-Madison, Madison, Wisconsin 53792, USA.
CONTRACT NUMBER: R01DC4428 (NIDCD)
SOURCE: The Annals of otology, rhinology, and laryngology, (2003 Jul) Vol. 112, No. 7, pp. 617-24.
Journal code: 0407300. ISSN: 0003-4894.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200308
ENTRY DATE: Entered STN: 8 Aug 2003
Last Updated on STN: 23 Aug 2003
Entered Medline: 22 Aug 2003

AB Hyaluronan (HYA) is considered to be a crucial factor in scarless wound healing and in maintaining tissue viscosity of the vocal fold lamina propria. In this study focusing on the effects of growth factors, we examined how HYA is produced and controlled in canine cultured vocal fold fibroblasts. Fibroblasts were taken from the lamina propria of the vocal folds of 8 dogs and cultured with and without growth factors. The production of HYA in the supernatant culture was quantitatively examined by enzyme-linked immunosorbent assay. Hepatocyte growth factor, epidermal growth factor, basic fibroblast growth factor, and transforming growth factor beta1 all stimulated HYA synthesis from vocal fold fibroblasts. These effects differed with the concentration of growth factors and the incubation period. We also examined how frequently the growth factors had to be administered in order to maintain appropriate levels of HYA. A single administration was sufficient to maintain appropriate HYA levels for at least 7 days. The present studies have demonstrated positive effects of growth factors in stimulating HYA production. Further in vivo study is needed to clarify the usefulness of these growth factors in the management of vocal fold scarring.

L1 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:480271 CAPLUS
DOCUMENT NUMBER: 119:80271
TITLE: Compositions containing fibroblast growth factor for treatment of the eyes
PATENT ASSIGNEE(S): Ramot University Authority for Applied Research and Industrial Development Ltd., Israel
SOURCE: Israeli, 16 pp.
CODEN: ISXXAQ
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
IL 82295	A1	19930221	IL 1987-82295	19870422
PRIORITY APPLN. INFO.:			IL 1987-82295	19870422

AB An ophthalmic preparation for enhancing regeneration of the corneal endothelium before and during surgery of the eye, for improving donor endothelium preservation prior to keratoplasty, and for use in cases of injury and disease, comprises fibroblast growth factor and a viscosity enhancer selected from hyaluronic acid, its salts, chondroitin sulfate, Me cellulose, and water-soluble collagens.

L1 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:537943 CAPLUS
DOCUMENT NUMBER: 131:161648
TITLE: Method of promoting bone growth with hyaluronic acid and growth factors
INVENTOR(S): Radomsky, Michael
PATENT ASSIGNEE(S): Orquest, Inc., USA
SOURCE: U.S., 12 pp., Cont.-in-part of U. S. Ser. No.611,690, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5942499	A	19990824	US 1997-811971	19970305
CN 1212628	A	19990331	CN 1997-192822	19970305
NZ 331238	A	20000526	NZ 1997-331238	19970305
US 6645945	B1	20031111	US 1999-298539	19990422
US 6221854	B1	20010424	US 1999-360543	19990726
US 2001014664	A1	20010816	US 2001-825688	20010403
US 6703377	B2	20040309		
US 2004176295	A1	20040909	US 2004-796441	20040308

PRIORITY APPLN. INFO.:

US 1996-611690	B2	19960305
US 1997-811971	A	19970305
WO 1997-US4810	W	19970305
US 1999-360543	A3	19990726
US 2001-825688	A1	20010403

AB A bone growth-promoting composition is provided comprising hyaluronic acid and a growth factor. The composition has a viscosity and biodegradability sufficient to persist at the site of desired bone growth for a period of time sufficient to promote the bone growth. Preferably hyaluronic acid is used in a composition range of 0.1-4 % and preferred growth factor is bFGF, present in a concentration range of about 10-6 to 100 mg/mL.
REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 1 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:887677 CAPLUS
DOCUMENT NUMBER: 139:333156
TITLE: Method of treating diseased, injured or abnormal cartilage with hyaluronic acid and a growth factor
INVENTOR(S): Radomsky, Michael; Heidaran, Mohammad A.
PATENT ASSIGNEE(S): DePuy Acromed, Inc., USA
SOURCE: U.S., 6 pp., Cont.-in-part of U.S. Ser. No. 811,971.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6645945	B1	20031111	US 1999-298539	19990422
US 5942499	A	19990824	US 1997-811971	19970305
PRIORITY APPLN. INFO.:			US 1996-611690	B2 19960305
			US 1997-811971	A2 19970305

AB A composition is provided for treating diseased, injured or diseased cartilage, comprising hyaluronic acid and a growth factor . The composition has a viscosity and biodegradability sufficient to persist at the site for a period sufficient to alleviate the symptoms of the disease, injury or abnormality. Preferably, hyaluronic acid is used in a composition range of 0.01-4% by weight and the preferred growth factor is IGF-I, present in a concentration range of about 10-6 to 100 mg/mL.
REFERENCE COUNT: 76 THERE ARE 76 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:294955 CAPLUS
DOCUMENT NUMBER: 134:290753
TITLE: Method of promoting bone growth with hyaluronic acid and growth factors
INVENTOR(S): Radomsky, Michael
PATENT ASSIGNEE(S): Orquest, Inc., USA
SOURCE: U.S., 11 pp., Cont.-in-part of U.S. 5,942,499.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6221854	B1	20010424	US 1999-360543	19990726
US 5942499	A	19990824	US 1997-811971	19970305
CA 2378328	AA	20010201	CA 2000-2378328	20000726
WO 2001007056	A1	20010201	WO 2000-US20373	20000726
WO 2001007056	C2	20020725		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1198235	A1	20020424	EP 2000-950736	20000726
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, SI, LT, LV, FI, RO, MK, CY, AL

JP 2003505422	T2	20030212	JP 2001-511940	20000726
NZ 516097	A	20040227	NZ 2000-516097	20000726
AU 777328	B2	20041014	AU 2000-63797	20000726
US 2001014664	A1	20010816	US 2001-825688	20010403
US 6703377	B2	20040309		
US 2004176295	A1	20040909	US 2004-796441	20040308
AU 2005200146	A1	20050210	AU 2005-200146	20050113

PRIORITY APPLN. INFO.:

US 1996-611690	B2	19960305
US 1997-811971	A2	19970305
US 1999-360543	A	19990726
WO 2000-US20373	W	20000726
US 2001-825688	A1	20010403

AB A bone growth-promoting composition is provided comprising hyaluronic acid and a growth factor. The composition has a viscosity and biodegradability sufficient to persist at an intra-articular site of desired bone growth for a period of time sufficient to promote the bone growth. Preferably hyaluronic acid is used in a composition range of 0.1-4% by weight and preferred growth factor is bFGF, present in a concentration range of about 10#-6 to 100 mg/mL.

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:78247 CAPLUS
DOCUMENT NUMBER: 134:125970
TITLE: Method of promoting bone growth with hyaluronic acid and growth factors
INVENTOR(S): Randomsky, Michael
PATENT ASSIGNEE(S): Orquest, Inc., USA
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001007056	A1	20010201	WO 2000-US20373	20000726
WO 2001007056	C2	20020725		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6221854	B1	20010424	US 1999-360543	19990726
CA 2378328	AA	20010201	CA 2000-2378328	20000726
EP 1198235	A1	20020424	EP 2000-950736	20000726
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003505422	T2	20030212	JP 2001-511940	20000726
NZ 516097	A	20040227	NZ 2000-516097	20000726
AU 777328	B2	20041014	AU 2000-63797	20000726
AU 2005200146	A1	20050210	AU 2005-200146	20050113

PRIORITY APPLN. INFO.:

US 1999-360543	A	19990726
US 1996-611690	B2	19960305
US 1997-811971	A2	19970305
WO 2000-US20373	W	20000726

AB A bone growth-promoting composition is provided comprising hyaluronic acid and a growth factor. The composition has a viscosity and biodegradability sufficient to persist at an intra-articular site of desired bone growth for a period of time sufficient to promote the bone growth. Preferably hyaluronic acid is used in a composition range of 0.1-4 % by weight and preferred growth factor is bFGF, present in a concentration range of about 10-6 to 100 mg/mL.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:640962 CAPLUS
DOCUMENT NUMBER: 131:271016
TITLE: Microorganisms secreting nucleases for control of medium viscosity in high density fermentation
INVENTOR(S): Huisman, Gjalt W.; Boynton, Laura; Horowitz, Daniel M.; Gerngross, Tillman U.; Peoples, Oliver P.
PATENT ASSIGNEE(S): Metabolix, Inc., USA
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9950389	A1	19991007	WO 1999-US6878	19990330
W: AU, CA, JP, MX				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2325350	AA	19991007	CA 1999-2325350	19990330
AU 9932157	A1	19991018	AU 1999-32157	19990330
AU 752620	B2	20020926		
EP 1068294	A1	20010117	EP 1999-914271	19990330
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002509714	T2	20020402	JP 2000-541277	19990330
US 2004014197	A1	20040122	US 2003-607903	20030627
PRIORITY APPLN. INFO.:			US 1998-79938P	P 19980330
			US 1999-281363	B3 19990330
			WO 1999-US6878	W 19990330
			US 1999-456940	A1 19991207

AB Microorganisms secreting nucleases (DNase or RNase) that can be used to control medium viscosity in fermentation at high cell d. are described. Expression constructs that can be used to improve production and recovery processes for polymers such as intracellular proteins, such as enzymes, growth factors, and cytokines; for producing polyhydroxyalkanoates; and for producing extracellular polysaccharides, such as xanthan gum, alginates, gellan gum, zooglan, hyaluronic acid and microbial cellulose are described. The nuc (nuclease) gene of Staphylococcus aureus was cloned into pUC18 and introduced into Pseudomonas putida and Ralstonia eutropha. Nuclease secreting transformants were selected on DNA agar plates. A secreting strain of P. putida was used to manufacture polyhydroxyalkanoates using an octanoic acid containing medium. Lystaes of cells were prepared using a high pressure homogenizer. The viscosity of lysates from nuclease secretors was comparable to, or lower than, that of lysates prepared with the com. nuclease Benzonase®.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:537943 CAPLUS
DOCUMENT NUMBER: 131:161648
TITLE: Method of promoting bone growth with hyaluronic acid and growth factors
INVENTOR(S): Radomsky, Michael
PATENT ASSIGNEE(S): Orquest, Inc., USA
SOURCE: U.S., 12 pp., Cont.-in-part of U. S. Ser. No.611,690, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5942499	A	19990824	US 1997-811971	19970305
CN 1212628	A	19990331	CN 1997-192822	19970305
NZ 331238	A	20000526	NZ 1997-331238	19970305
US 6645945	B1	20031111	US 1999-298539	19990422
US 6221854	B1	20010424	US 1999-360543	19990726
US 2001014664	A1	20010816	US 2001-825688	20010403
US 6703377	B2	20040309		
US 2004176295	A1	20040909	US 2004-796441	20040308

PRIORITY APPLN. INFO.:
US 1996-611690 B2 19960305
US 1997-811971 A 19970305
WO 1997-US4810 W 19970305
US 1999-360543 A3 19990726
US 2001-825688 A1 20010403

AB A bone growth-promoting composition is provided comprising hyaluronic acid and a growth factor. The composition has a viscosity and biodegradability sufficient to persist at the site of desired bone growth for a period of time sufficient to promote the bone growth. Preferably hyaluronic acid is used in a composition range of 0.1-4 % and preferred growth factor is bFGF, present in a concentration range of about 10-6 to 100 mg/mL.

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:617981 CAPLUS
DOCUMENT NUMBER: 127:253211
TITLE: Method of promoting bone growth with hyaluronic acid and growth factors
INVENTOR(S): Radomsky, Michael
PATENT ASSIGNEE(S): Orquest, Inc., USA
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9732591	A1	19970912	WO 1997-US4810	19970305
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, YU				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2246747	AA	19970912	CA 1997-2246747	19970305

AU 9725449	A1	19970922	AU 1997-25449		19970305
AU 729086	B2	20010125			
CN 1212628	A	19990331	CN 1997-192822		19970305
EP 910389	A1	19990428	EP 1997-916976		19970305
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
NZ 331238	A	20000526	NZ 1997-331238		19970305
JP 2002504083	T2	20020205	JP 1997-532070		19970305
PRIORITY APPLN. INFO.:			US 1996-611690	A	19960305
			US 1997-811971	A	19970305
			WO 1997-US4810	W	19970305

AB A bone growth-promoting composition is provided comprising hyaluronic acid and a growth factor. The composition has a viscosity and biodegradability sufficient to persist at the site of desired bone growth for a period of time sufficient to promote the bone growth. Preferably hyaluronic acid is used in a composition range of 0.1 to 4 % and preferred growth factor is bFGF, present in a concentration range of 10-6 to 100 mg/mL. An aqueous solution containing Na hyaluronate, bFGF, and Na citrate was injected with a needle between the periosteum and parietal bone of rats. The animals were euthanized 14 days following treatment and new bone formation was evaluated.

L1 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:332901 CAPLUS
DOCUMENT NUMBER: 125:19048
TITLE: Fibroblast growth factors for the treatment of eye diseases
INVENTOR(S): Belkin, Michael; Savion, Naphtali; Landshman, Nahum
PATENT ASSIGNEE(S): Ramot University for Applied Research and Industrial Development Ltd., Israel
SOURCE: U.S., 9 pp., Cont. of U.S. Ser. 673, 867, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 5510329	A	19960423	US 1992-997664		19921228
PRIORITY APPLN. INFO.:			US 1992-997664	B1	19921228
			US 1991-673867	B1	19910322
			US 1988-185893		19880426

AB The invention relates to compns. which induce regeneration of the corneal endothelium. The compns. are of value in regenerating the corneal endothelium in humans, which is frequently damaged in the course of eye surgery and injuries. Such regeneration is very important to ensure the full functionality of the eye. The compns. comprise as active ingredient an adequate quantity of fibroblast growth factor in a suitable physiol. acceptable vehicle. A preferred embodiment of the invention relates to a composition containing a certain quantity of hyaluronic acid and any other viscoelastic agent.

L1 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:480271 CAPLUS
DOCUMENT NUMBER: 119:80271
TITLE: Compositions containing fibroblast growth factor for treatment of the eyes
PATENT ASSIGNEE(S): Ramot University Authority for Applied Research and Industrial Development Ltd., Israel
SOURCE: Israeli, 16 pp.
CODEN: ISXXAQ

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
IL 82295	A1	19930221	IL 1987-82295	19870422
PRIORITY APPLN. INFO.:			IL 1987-82295	19870422

AB An ophthalmic preparation for enhancing regeneration of the corneal endothelium before and during surgery of the eye, for improving donor endothelium preservation prior to keratoplasty, and for use in cases of injury and disease, comprises fibroblast growth factor and a viscosity enhancer selected from hyaluronic acid, its salts, chondroitin sulfate, Me cellulose, and water-soluble collagens.

L1 ANSWER 9 OF 10 MEDLINE on STN
ACCESSION NUMBER: 2004115350 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15005294
TITLE: Understanding osteoarthritis of the knee--causes and effects.
AUTHOR: Moskowitz Roland W; Kelly Michael A; Lewallen David G
CORPORATE SOURCE: Case Western Reserve University School of Medicine in Cleveland, Ohio, USA.
SOURCE: American journal of orthopedics (Belle Mead, N.J.), (2004 Feb) Vol. 33, No. 2 Suppl, pp. 5-9.
Journal code: 9502918. ISSN: 1078-4519.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200405
ENTRY DATE: Entered STN: 10 Mar 2004
Last Updated on STN: 26 May 2004
Entered Medline: 25 May 2004

AB Osteoarthritis of the knee is common, increasing with age in both women and men, but is generally more prevalent in women following the fourth decade. Osteoarthritis may be primary/idiopathic or secondary as a consequence of trauma, surgery, infection, or another disease process. Normal articular cartilage is composed of an extracellular matrix and chondrocytes. This matrix contains water, collagen fibers, and proteoglycan macromolecules cross-linked into an integrated network with hyaluronic acid. Osteoarthritis represents an imbalance in the destructive and synthetic processes of the cartilage that leads to erosion of the cartilage. In addition, there is a decreased concentration and viscosity of the synovial fluid in osteoarthritic patients, and this may decrease the lubricating and cushioning properties of the joint. There is also an underlying inflammation of the synovium, as well as damage or reactive changes in the subchondral bone. The entire process is thought to involve a complex interaction of cells and soluble mediators such as cytokines, growth factors, inflammatory mediators, metalloproteinases, and chondrodegradative enzymes. Understanding the biochemical and molecular changes that occur in the joint is requisite to the development of treatments for osteoarthritis of the knee that address both the symptoms of pain and loss of mobility as well as the underlying disease progression. The clinical goal of the management of osteoarthritis should be to treat not only the symptoms of the disease, such as pain and decreased mobility, but also the underlying pathology of the degenerative process.

L1 ANSWER 10 OF 10 MEDLINE on STN
ACCESSION NUMBER: 2003369126 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12903682
TITLE: Effect of growth factors on hyaluronan production by canine

vocal fold fibroblasts.

AUTHOR: Hirano Shigeru; Bless Diane M; Heisey Dennis; Ford Charles N

CORPORATE SOURCE: Department of Surgery, Division of Otolaryngology-Head and Neck Surgery, University of Wisconsin-Madison, Madison, Wisconsin 53792, USA.

CONTRACT NUMBER: R01DC4428 (NIDCD)

SOURCE: The Annals of otology, rhinology, and laryngology, (2003 Jul) Vol. 112, No. 7, pp. 617-24.
Journal code: 0407300. ISSN: 0003-4894.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals

ENTRY MONTH: 200308

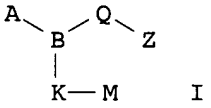
ENTRY DATE: Entered STN: 8 Aug 2003
Last Updated on STN: 23 Aug 2003
Entered Medline: 22 Aug 2003

AB Hyaluronan (HYA) is considered to be a crucial factor in scarless wound healing and in maintaining tissue viscosity of the vocal fold lamina propria. In this study focusing on the effects of growth factors, we examined how HYA is produced and controlled in canine cultured vocal fold fibroblasts. Fibroblasts were taken from the lamina propria of the vocal folds of 8 dogs and cultured with and without growth factors. The production of HYA in the supernatant culture was quantitatively examined by enzyme-linked immunosorbent assay. Hepatocyte growth factor, epidermal growth factor, basic fibroblast growth factor, and transforming growth factor beta1 all stimulated HYA synthesis from vocal fold fibroblasts. These effects differed with the concentration of growth factors and the incubation period. We also examined how frequently the growth factors had to be administered in order to maintain appropriate levels of HYA. A single administration was sufficient to maintain appropriate HYA levels for at least 7 days. The present studies have demonstrated positive effects of growth factors in stimulating HYA production. Further in vivo study is needed to clarify the usefulness of these growth factors in the management of vocal fold scarring.

L5 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:434351 CAPLUS
DOCUMENT NUMBER: 139:26619
TITLE: Pharmaceutical compositions containing EP2 receptor selective agonists for treatment of bone disease
INVENTOR(S): Dumont, Francis; Hong, Jinyang; Kim, Yesook; Korsmeyer, Richard Wilker; Li, Mei; Paralkar, Vishwas Madhav; Thompson, David Duane
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 76 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2003045371	A1	20030605	WO 2002-IB4368		20021021
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2468494	AA	20030605	CA 2002-2468494		20021021
AU 2002348948	A1	20030610	AU 2002-348948		20021021
EP 1448182	A1	20040825	EP 2002-781458		20021021
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK					
BR 2002014614	A	20040914	BR 2002-14614		20021021
CN 1599605	A	20050323	CN 2002-823938		20021021
JP 2005513030	T2	20050512	JP 2003-546873		20021021
US 2003166631	A1	20030904	US 2002-305649		20021126
ZA 2004002795	A	20050413	ZA 2004-2795		20040413
NO 2004002272	A	20040728	NO 2004-2272		20040601
PRIORITY APPLN. INFO.:			US 2001-335156P	P	20011130
			WO 2002-IB4368	W	20021021

OTHER SOURCE(S): MARPAT 139:26619
GI



I

AB This invention is directed to pharmaceutical compns. and methods comprising prostaglandin agonists, specifically EP2 receptor selective agonists, which are useful to enhance bone repair and healing and restore or augment bone mass in vertebrates, particularly mammals. The EP2 receptor selective agonists of the present invention are effective in the treatment of conditions such as those in which the patient has delayed or non-union fracture, bone defect, spinal fusion, bone in-growth, cranial facial reconstruction or bone sites at risk for fracture. E.g., an EP2 agonist such as I is formulated in vehicles such as Pluronic F127.

Hyaluronic acid and growth factors may also be incorporated into the formulations.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:278267 CAPLUS
DOCUMENT NUMBER: 135:255234
TITLE: Abnormalities of bone marrow mesenchymal cells in multiple myeloma patients
AUTHOR(S): Wallace, Stephanie R.; Oken, Martin M.; Lunetta, Kathryn L.; Panoskaltsis-Mortari, Angela; Masellis, Anna M.
CORPORATE SOURCE: Virginia Piper Cancer Institute, Abbott Northwestern Hospital, Minneapolis, MN, 55407, USA
SOURCE: Cancer (New York, NY, United States) (2001), 91(7), 1219-1230
CODEN: CANCAR; ISSN: 0008-543X
PUBLISHER: John Wiley & Sons, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The importance of the bone marrow microenvironment in multiple myeloma is receiving increasing attention. Recent studies have suggested the importance of cytokine production and cell-cell contact by bone marrow stromal cells in the survival of myeloma cells. In the current study, the authors examined bone marrow mesenchymal progenitor cell (MPC) cultures derived from 8 multiple myeloma patients (mean age, 58 yr) and 9 normal donors (mean age, 61 yr), with emphasis on cell surface antigens, cytokine, and growth factor expression. The authors have found, based on anal. of cellular receptors, growth factors, and cytokine expression, that myeloma MPCs are phenotypically and functionally distinguishable from normal donor MPCs. Immunofluorescence anal. of MPC monolayers shows that myeloma MPC cultures expressed reduced cell surface vascular cell adhesion mol.-1 and fibronectin, in contrast with the strong expression found on normal donor MPCs. Furthermore, a subset of myeloma MPCs strongly express intracellular receptor for hyaluronan-mediated motility, whereas normal MPCs do not. Cytokine expression in bone marrow MPC cultures was examined by reverse transcription-polymerase chain reaction and enzyme linked immunosorbent assay. Bone marrow MPCs constitutively express interleukin (IL)-1β, IL-6, granulocyte colony-stimulating factor (G-CSF), granulocyte macrophage (GM)-CSF, stem cell factor (SCF), and tumor necrosis factor (TNF)-α.. In comparison to normal MPCs, multiple myeloma MPCs express increased basal levels of IL-1β and TNF-α. In vitro exposure of MPC cultures to dexamethasone resulted in the down-regulation of IL-6, G-CSF, and GM-CSF in both normal and myeloma MPC cultures. However, dexamethasone treatment significantly increased expression of SCF-1 in myeloma MPCs. In myeloma, bone marrow stromal cells provide paracrine factors, through cytokine production and cell-cell contact, which play a role in plasma cell growth and survival. The authors' data indicate differences in bone marrow MPCs, which may be biol. relevant to the growth and survival of myeloma plasma cells.

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:433930 CAPLUS
DOCUMENT NUMBER: 127:131475
TITLE: Age-related changes in effects of insulin-like growth factor I on human osteoblast-like cells
AUTHOR(S): d'Avis, Patricia Y.; Frazier, Chester R.; Shapiro, Jay R.; Fedarko, Neal S.
CORPORATE SOURCE: Division Geriatrics, Department Medicine, Johns

Hopkins University School Medicine, Baltimore, MD, 21224, USA
SOURCE: Biochemical Journal (1997), 324(3), 753-760
CODEN: BIJOAK; ISSN: 0264-6021
PUBLISHER: Portland Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The role of insulin-like growth factor I (IGF-I) in extracellular matrix metabolism was studied in both proliferating and confluent human osteoblast-like cultures derived from donors of different ages. In proliferating cultures, recombinant human (rh)IGF-I was found to increase the incorporation of [3H]thymidine in a dose- and age-dependent manner. To study cell proliferation dynamically, continuous growth curves with and without rhIGF-I were modeled by a modified logistic function. Increasing doses of rhIGF-I decreased the lag time and maximal growth rates, whereas plateau values decreased only at the highest dose (100 ng/mL). In post-proliferative cell strains, rhIGF-I (0.1-100 ng/mL) increased levels of type I collagen, biglycan and decorin, and to a smaller extent fibronectin and thrombospondin, whereas it decreased the levels of hyaluronan and a versican-like proteoglycan when protein and proteoglycan metabolism were followed by steady-state radiolabeling with [3H]proline, [3H]glucosamine or [35S]sulfate. These responses to rhIGF-I were found to be age-dependent, with osteoblast-like cells derived from younger patients being more responsive to rhIGF-I. When extracellular matrix turnover was analyzed by pulse-chase expts., rhIGF-I had no effect. The steady-state levels of collagen, decorin, hyaluronan and a versican-like proteoglycan for bone cells treated with rhIGF-I on day 7 in culture were equivalent to levels of these matrix components in untreated osteoblasts grown for 14 days. These results are consistent with rhIGF-I's altering cellular proliferative capacity and matrix synthesis, causing a change in the osteoblast differentiated state.

L5 ANSWER 4 OF 6 MEDLINE on STN
ACCESSION NUMBER: 2004115350 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15005294
TITLE: Understanding osteoarthritis of the knee--causes and effects.
AUTHOR: Moskowitz Roland W; Kelly Michael A; Lewallen David G
CORPORATE SOURCE: Case Western Reserve University School of Medicine in Cleveland, Ohio, USA.
SOURCE: American journal of orthopedics (Belle Mead, N.J.), (2004 Feb) Vol. 33, No. 2 Suppl, pp. 5-9.
Journal code: 9502918. ISSN: 1078-4519.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200405
ENTRY DATE: Entered STN: 10 Mar 2004
Last Updated on STN: 26 May 2004
Entered Medline: 25 May 2004

AB Osteoarthritis of the knee is common, increasing with age in both women and men, but is generally more prevalent in women following the fourth decade. Osteoarthritis may be primary/idiopathic or secondary as a consequence of trauma, surgery, infection, or another disease process. Normal articular cartilage is composed of an extracellular matrix and chondrocytes. This matrix contains water, collagen fibers, and proteoglycan macromolecules cross-linked into an integrated network with hyaluronic acid. Osteoarthritis represents an imbalance in the destructive and synthetic processes of the cartilage that leads to erosion of the cartilage. In addition, there is a decreased concentration and viscosity of the synovial fluid in osteoarthritic patients, and this may decrease the lubricating and cushioning properties of the joint.

There is also an underlying inflammation of the synovium, as well as damage or reactive changes in the subchondral bone. The entire process is thought to involve a complex interaction of cells and soluble mediators such as cytokines, growth factors, inflammatory mediators, metalloproteinases, and chondrodegradative enzymes. Understanding the biochemical and molecular changes that occur in the joint is requisite to the development of treatments for osteoarthritis of the knee that address both the symptoms of pain and loss of mobility as well as the underlying disease progression. The clinical goal of the management of osteoarthritis should be to treat not only the symptoms of the disease, such as pain and decreased mobility, but also the underlying pathology of the degenerative process.

L5 ANSWER 5 OF 6 MEDLINE on STN
ACCESSION NUMBER: 2001236820 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11283920
TITLE: Abnormalities of bone marrow mesenchymal cells in multiple myeloma patients.
AUTHOR: Wallace S R; Oken M M; Lunetta K L; Panoskaltsis-Mortari A; Masellis A M
CORPORATE SOURCE: Virginia Piper Cancer Institute, Abbott Northwestern Hospital, Minneapolis, Minnesota, USA.
SOURCE: Cancer, (2001 Apr 1) Vol. 91, No. 7, pp. 1219-30. Journal code: 0374236. ISSN: 0008-543X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 17 May 2001
Last Updated on STN: 17 May 2001
Entered Medline: 3 May 2001

AB BACKGROUND: The importance of the bone marrow microenvironment in multiple myeloma is receiving increasing attention. Recent studies have suggested the importance of cytokine production and cell-cell contact by bone marrow stromal cells in the survival of myeloma cells. METHODS: In the current study, the authors examined bone marrow mesenchymal progenitor cell (MPC) cultures derived from eight multiple myeloma patients (mean age, 58 years) and nine normal donors (mean age, 61 years), with emphasis on cell surface antigens, cytokine, and growth factor expression. RESULTS: The authors have found, based on analysis of cellular receptors, growth factors, and cytokine expression, that myeloma MPCs are phenotypically and functionally distinguishable from normal donor MPCs. Immunofluorescence analysis of MPC monolayers shows that myeloma MPC cultures expressed reduced cell surface vascular cell adhesion molecule-1 and fibronectin, in contrast with the strong expression found on normal donor MPCs. Furthermore, a subset of myeloma MPCs strongly express intracellular receptor for hyaluronan-mediated motility, whereas normal MPCs do not. Cytokine expression in bone marrow MPC cultures was examined by reverse transcription-polymerase chain reaction and enzyme linked immunosorbent assay. Bone marrow MPCs constitutively express interleukin (IL)-1beta, IL-6, granulocyte colony-stimulating factor (G-CSF), granulocyte macrophage (GM)-CSF, stem cell factor (SCF), and tumor necrosis factor (TNF)-alpha. In comparison to normal MPCs, multiple myeloma MPCs express increased basal levels of IL-1beta and TNF-alpha. In vitro exposure of MPC cultures to dexamethasone resulted in the down-regulation of IL-6, G-CSF, and GM-CSF in both normal and myeloma MPC cultures. However, dexamethasone treatment significantly increased expression of SCF-1 in myeloma MPCs. CONCLUSIONS: In myeloma, bone marrow stromal cells provide paracrine factors, through cytokine production and cell-cell contact, which play a role in plasma cell growth and survival. The authors' data indicate differences in bone marrow MPCs, which

may be biologically relevant to the growth and survival of myeloma plasma cells.

L5 ANSWER 6 OF 6 MEDLINE on STN

ACCESSION NUMBER: 97327721 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9210398
TITLE: Age-related changes in effects of insulin-like growth factor I on human osteoblast-like cells.
AUTHOR: D'avis P Y; Frazier C R; Shapiro J R; Fedarko N S
CORPORATE SOURCE: Division of Geriatrics, Department of Medicine, Room 5A-50 JHAAC, Johns Hopkins University School of Medicine, 5501 Hopkins Bayview Circle, Baltimore, MD 21224, USA.
CONTRACT NUMBER: AR 42358 (NIAMS)
SOURCE: The Biochemical journal, (1997 Jun 15) Vol. 324 (Pt 3), pp. 753-60.
Journal code: 2984726R. ISSN: 0264-6021.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199707
ENTRY DATE: Entered STN: 12 Aug 1997
Last Updated on STN: 12 Aug 1997
Entered Medline: 28 Jul 1997

AB The role of insulin-like growth factor I (IGF-I) in extracellular matrix metabolism was studied in both proliferating and confluent human osteoblast-like cultures derived from donors of different ages. In proliferating cultures, recombinant human (rh)IGF-I was found to increase the incorporation of [3H]thymidine in a dose- and age-dependent manner. To study cell proliferation dynamically, continuous growth curves with and without rhIGF-I were modelled by a modified logistic function. Increasing doses of rhIGF-I decreased the lag time and maximal growth rates, whereas plateau values decreased only at the highest dose (100 ng/ml). In post-proliferative cell strains, rhIGF-I (0.1-100 ng/ml) increased levels of type I collagen, biglycan and decorin, and to a smaller extent fibronectin and thrombospondin, whereas it decreased the levels of hyaluronan and a versican-like proteoglycan when protein and proteoglycan metabolism were followed by steady-state radiolabelling with [3H]proline, [3H]glucosamine or [35S]sulphate. These responses to rhIGF-I were found to be age-dependent, with osteoblast-like cells derived from younger patients being more responsive to rhIGF-I. When extracellular matrix turnover was analysed by pulse-chase experiments, rhIGF-I had no effect. The steady-state levels of collagen, decorin, hyaluronan and a versican-like proteoglycan for bone cells treated with rhIGF-I on day 7 in culture were equivalent to levels of these matrix components in untreated osteoblasts grown for 14 days. These results are consistent with rhIGF-I's altering cellular proliferative capacity and matrix synthesis, causing a change in the osteoblast differentiated state.

L6 ANSWER 10 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:351063 CAPLUS
DOCUMENT NUMBER: 125:30892
TITLE: Basic fibroblast growth factor enhances bone-graft incorporation: Dose and time dependence in rats
AUTHOR(S): Wang, Jian-Sheng; Aspenberg, Per
CORPORATE SOURCE: Department Orthopedics, Lund University Hospital, Lund, S-22185, Swed.
SOURCE: Journal of Orthopaedic Research (1996), 14(2), 316-323
CODEN: JOREDR; ISSN: 0736-0266
PUBLISHER: Journal of Bone and Joint surgery, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In a previous study, we found that basic fibroblast growth factor could stimulate bone-graft incorporation. In the present study, the effects of different doses and implantation times were further studied, using the bone conduction chamber, in rats. Inside the chamber, the graft is isolated from the surrounding tissues except at one end, where small openings embedded in host bone allow ingrowth of tissue. The distance that new tissues had reached from the openings into the graft was measured on histol. slides. Bone grafts were obtained from the proximal tibiae of donor rats, frozen at -70°C, and lipid-extracted Before implantation, they were soaked overnight in a hyaluronate gel with or without basic fibroblast growth factor and then were fitted into the chambers, which were implanted in the proximal tibiae of recipient rats. In a dose response experiment, grafts containing 0.3, 8, 40, 200, or 1,000 ng of basic fibroblast growth factor were compared with grafts treated with carrier gel only, after an implantation time of 6 wk. Fibrous tissue always penetrated the grafts further than the ingrown bone; the distance that it reached from the ingrowth openings (total ingrowth distance) was increased by all of the doses except 0.3 ng per implant. The distance of bone ingrowth was increased by 8, 40, and 200 ng. The increased total ingrowth with 1,000 ng was due to an increased amount of fibrous tissue ahead of the bone, whereas with the lower doses the increase was due to more bone. Thus, the dose had an effect on the type of ingrown tissue found in the graft. In a time-effect study, grafts treated with 40 ng of basic fibroblast growth factor had a higher uptake of [99mTc]MDP at 2 and 4 wk and an increased bone ingrowth distance at 10 wk. The radioactivity from [125I]basic fibroblast growth factor declined with a half-life of 17 h. The results suggest that basic fibroblast growth factor may be beneficial for the incorporation of contained bone grafts; studies using more clin. relevant models are required.

L6 ANSWER 11 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:571362 CAPLUS
DOCUMENT NUMBER: 121:171362
TITLE: Transforming growth factor-β stimulates retinoic acid-induced proteoglycan depletion in intact articular cartilage
AUTHOR(S): Von den Hoff, Hans W.; de Koning, Margret H. M. T.; Jos van Kampen, G. P.; van der Korst, Jan K.
CORPORATE SOURCE: Jan van Breemen Inst., Cent. Rheumatology Rehabilitation, Amsterdam, Neth.
SOURCE: Archives of Biochemistry and Biophysics (1994), 313(2), 241-7
CODEN: ABBIA4; ISSN: 0003-9861
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Cartilage-bearing sesamoid bones from the metacarpophalangeal joints of adult cows were cultured with retinoic acid for 1 wk and allowed

to recover in control medium for another 2 wk. Retinoic acid decreased the proteoglycan synthesis of the cartilage to 33% of control values, and induced 26% loss of proteoglycans from the matrix. During recovery, the synthesis of proteoglycans returned to the control level but their content remained reduced. Transforming growth factor-β (TGF-β1, 5 ng/mL) was added to the culture medium to stimulate the recovery. However, TGF-β depressed the synthesis of proteoglycans and increased their loss to 61%. Only the large aggregating species, aggrecan, was lost from the matrix. The half-life of proteoglycans synthesized during recovery in control medium was 12.7 days, which was reduced to 8.7 days by TGF-β. The proteoglycan half-life in control cartilage cultured without retinoic acid or TGF-β was 33.8 days. Neither retinoic acid nor TGF-β-induced changes in the hyaluronate content of the tissue. Aggrecans and small proteoglycans synthesized in the presence of TGF-β were larger than those in controls. The synthesis of the small proteoglycans was stimulated 4.5-fold by TGF-β, and their content was increased. The results show that TGF-β can stimulate depletion of aggrecan in retinoic acid-treated cartilage. This indicates a catabolic function of TGF-β in cartilage remodeling.

L6 ANSWER 12 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:45790 CAPLUS
DOCUMENT NUMBER: 118:45790
TITLE: Pharmaceutical compositions containing bioactive peptides for virus inhibition and wound healing
INVENTOR(S): Miyoshi, Teruzo; Mimura, Shuji
PATENT ASSIGNEE(S): Denki Kagaku Kogyo K. K., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 6 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 04282322	A2	19921007	JP 1991-67665	19910308

PRIORITY APPLN. INFO.: JP 1991-67665 19910308

AB A pharmaceutical contains a transforming growth factor 10 μg, and 0.5 weight% Na hyaluronate in 100 mL saline (pH 7.1). Bioactive peptides may be a proteinase such as trypsin inhibitor. The preparation is effective in treating virus infection, aging, wounds, inflammations, and bone diseases. Biopolymers such as atelocollagen may be incorporated into the compns.

L6 ANSWER 13 OF 23 MEDLINE on STN
ACCESSION NUMBER: 2006240381 IN-PROCESS
DOCUMENT NUMBER: PubMed ID: 16575912
TITLE: Porous gelatin-chondroitin-hyaluronate tri-copolymer scaffold containing microspheres loaded with TGF-beta1 induces differentiation of mesenchymal stem cells in vivo for enhancing cartilage repair.
AUTHOR: Fan Hongbin; Hu Yunyu; Qin Ling; Li Xusheng; Wu Hong; Lv Rong
CORPORATE SOURCE: Institute of Orthopaedics and Traumatology, Xijing Hospital, The Fourth Military Medical University, Xi'an, People's Republic of China.
SOURCE: Journal of biomedical materials research. Part A, (2006 Jun 15) Vol. 77, No. 4, pp. 785-94.
Journal code: 101234237. ISSN: 1549-3296.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English

FILE SEGMENT: NONMEDLINE; IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 2 May 2006
Last Updated on STN: 9 Jun 2006

AB The aim of the study was to produce a novel porous gelatin-chondroitin-hyaluronate scaffold in combination with a controlled release of transforming growth factor beta1 (TGF-beta1), which induced the differentiation of mesenchymal stem cells (MSCs) in vivo for enhancing cartilage repair. Gelatin microspheres loaded with TGF-beta1 (MS-TGFbeta1) showed a fast release at the initial phase (37.4%), and the ultimate accumulated release was 83.1% by day 18. The autologous MSCs seeded on MS-TGFbeta1/scaffold were implanted to repair full-thickness cartilage defects in rabbits as in vivo differentiation repair group, while MSCs differentiated in vitro were seeded on scaffold without MS-TGFbeta1 to repair the contra lateral cartilage defects (n = 30). Fifteen additional rabbits without treatment for defects were used as control. Histology observation showed that the in vivo differentiation repair group had better chondrocyte morphology, integration, continuous subchondral bone, and much thicker newly formed cartilage layer when compared to in vitro differentiation repair group 12 and 24 weeks, postoperatively. There was a significant difference in histological grading score between these two experimental groups, and both showed much better repair than that of the control. The present study implied that the novel scaffold with MS-TGFbeta1 might serve as a new way to induce the differentiation of MSCs in vivo to enhance the cartilage repair.

L6 ANSWER 14 OF 23 MEDLINE on STN
ACCESSION NUMBER: 2005484540 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15967685
TITLE: Regeneration of articular cartilage--evaluation of osteochondral defect repair in the rabbit using multiphasic implants.
AUTHOR: Frenkel S R; Bradica G; Brekke J H; Goldman S M; Ieska K; Issack P; Bong M R; Tian H; Gokhale J; Coutts R D; Kronengold R T
CORPORATE SOURCE: Musculoskeletal Research Center, Department of Orthopedic Surgery, New York University-Hospital for Joint Diseases, New York, NY 10003, USA.. sallyfrenkel@yahoo.com
SOURCE: Osteoarthritis and cartilage / OARS, Osteoarthritis Research Society, (2005 Sep) Vol. 13, No. 9, pp. 798-807. Journal code: 9305697. ISSN: 1063-4584.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200601
ENTRY DATE: Entered STN: 13 Sep 2005
Last Updated on STN: 18 Jan 2006
Entered Medline: 17 Jan 2006

AB OBJECTIVE: To investigate whether two different multiphasic implants could initiate and sustain repair of osteochondral defects in rabbits. The implants address the malleable properties of cartilage while also addressing the rigid characteristics of subchondral bone. DESIGN: The bone region of both devices consisted of D, D-L, L-polylactic acid invested with hyaluronan (HY). The cartilage region of the first device was a polyelectrolytic complex (PEC) hydrogel of HY and chitosan. In the second device the cartilage region consisted of type I collagen scaffold. Eighteen rabbits were implanted bilaterally with a device, or underwent defect creation with no implant. At 24 weeks, regenerated tissues were evaluated grossly, histologically and via immunostaining for type II collagen. RESULTS: PEC devices induced a significantly better repair than untreated shams. Collagen devices resulted in a quality of repair close to that of the PEC group, although its mean repair score (19.0+/-4.2) did not differ significantly from that

of the PEC group (20.4+/-3.7) or the shams (16.5+/-6.3). The percentage of hyaline-appearing cartilage in the repair was highest with collagen implants, while the degree of bonding of repair to the host, structural integrity of the neocartilage, and reconstitution of the subchondral bone was greatest with PEC devices. Cartilage in both device-treated sites stained positive for type II collagen and GAG. CONCLUSIONS: Both implants are capable of maintaining hyaline-appearing tissue at 24 weeks. The physicochemical region between the cartilage and bone compartments makes these devices well suited for delivery of different growth factors or drugs in each compartment, or different doses of the same factor. It also renders these devices excellent vehicles for chondrocyte or stem cell transplantation.

L6 ANSWER 15 OF 23 MEDLINE on STN
ACCESSION NUMBER: 2003381100 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12916297
TITLE: Experimental study of repairing segmental bone defect with reconstituted freeze-dried bone allograft.
AUTHOR: Chen Qing; Gu Jie-fu; Cai Lin
CORPORATE SOURCE: Department of Orthopedic Surgery, Central Hospital of Wuhan, Wuhan, Hubei, P. R. China 430014.
SOURCE: Zhongguo xiu fu chong jian wai ke za zhi = Zhongguo xiufu chongjian waike zazhi = Chinese journal of reparative and reconstructive surgery, (2003 Jan) Vol. 17, No. 1, pp. 5-8. Journal code: 9425194. ISSN: 1002-1892.
PUB. COUNTRY: China
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Chinese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200312
ENTRY DATE: Entered STN: 15 Aug 2003
Last Updated on STN: 18 Dec 2003
Entered Medline: 17 Dec 2003
AB OBJECTIVE: To study the effect of basic fibroblast growth factor (bFGF) and hyaluronic acid gel (HAG) combined with freeze-dried bone allograft in repairing segmental bone defect and to explore their mechanism. METHODS: The 15 mm segmental bone/periosteum defects were created on bilateral radius in 50 New Zealand rabbits and were treated with four different kinds of implants on 25 radius respectively (group A: bFGF and HAG combined with freeze-dried bone; group B: bFGF combined with freeze-dried bone; group C: HAG combined with freeze-dried bone; group D: simple freeze-dried bone as a control). The repair of defect was observed radiologically and histologically and were analyzed by radionuclide bone imaging and measurement of calcium contents at different periods. RESULTS: The new bone formation, bone metabolic activity and calcium contents of defects were higher in group A than in group B ($P < 0.05$), and were higher in group B than in groups C and D ($P < 0.05$). There were no significant difference between groups C and D. The bone defects healed in the 8th week in group A, in the 10th week in group B, but did not healed in the 10th week in groups C and D. CONCLUSION: As an osteogenetic factor, bFGF promotes the new bone formation; as a slow-release carrier, HAG enhances the effectiveness of bFGF. The combination of bFGF, HAG and freeze-dried bone allograft can repair the segmental bone defect more effectively.

L6 ANSWER 16 OF 23 MEDLINE on STN
ACCESSION NUMBER: 2001653984 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11696432
TITLE: Anti-inflammatory and chondroprotective effect of TSG-6 (tumor necrosis factor-alpha-stimulated gene-6) in murine models of experimental arthritis.
AUTHOR: Bardos T; Kamath R V; Mikecz K; Glant T T

CORPORATE SOURCE: Department of Orthopedic Surgery, Section of Biochemistry and Molecular Biology, Rush University, Rush-Presbyterian-St. Luke's Medical Center, Chicago, Illinois 60612, USA.
CONTRACT NUMBER: AR40310 (NIAMS)
AR45652 (NIAMS)
AR47135 (NIAMS)
SOURCE: The American journal of pathology, (2001 Nov) Vol. 159, No. 5, pp. 1711-21.
Journal code: 0370502. ISSN: 0002-9440.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 15 Nov 2001
Last Updated on STN: 4 Apr 2002
Entered Medline: 7 Dec 2001

AB Tumor necrosis factor-alpha (TNF-alpha)-stimulated gene-6 (TSG-6) is up-regulated by various cytokines and growth factors. TSG-6 binds to hyaluronan in inflamed synovial tissue and forms a complex with a serine protease inter-alpha-trypsin inhibitor (IalphaI), increasing the protease inhibitory effect of IalphaI >100-fold. The TSG-6/IalphaI complex then blocks serine proteases, including the plasminogen-plasmin activation, probably the most important component in the activation processes of matrix metalloproteinases. To gain insight into the mechanisms of TSG-6 action in arthritis, we have used an autoimmune murine model (proteoglycan-induced arthritis) for systemic, and a monoarticular form of arthritis (antigen-induced arthritis) for local treatment of arthritis with recombinant mouse TSG-6 (rmTSG-6). Intravenous injection of rmTSG-6 induced a dramatic reduction of edema in acutely inflamed joints by immobilizing CD44-bound hyaluronan and, in long-term treatment, protected cartilage from degradation and blocked subchondral and periosteal bone erosion in inflamed joints. The intra-articular injection of a single dose (100 microg) of rmTSG-6 exhibited a strong chondroprotective effect for up to 5 to 7 days, preventing cartilage proteoglycan from metalloproteinase-induced degradation. In contrast, rmTSG-6 did not postpone the onset, nor reduce the incidence of arthritis. We were unable to detect any significant differences between control and rmTSG-6-treated animals when various serum markers (including pro- and anti-inflammatory cytokines, auto- and heteroantibody productions) or antigen-specific T-cell responses were compared, nor when the expressions of numerous cell surface receptors or adhesion molecules were measured. TSG-6 seems to play a critical negative regulatory feed-back function in inflammation, especially in arthritic processes.

L6 ANSWER 17 OF 23 MEDLINE on STN
ACCESSION NUMBER: 2000461432 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10834548
TITLE: Effects of platelet-derived growth factor-AA on the healing process of tympanic membrane perforation.
AUTHOR: Yeo S W; Kim S W; Suh B D; Cho S H
CORPORATE SOURCE: Department of Otolaryngology-Head and Neck Surgery, The Catholic University of Korea, College of Medicine, Seoul, Korea.
SOURCE: American journal of otolaryngology, (2000 May-Jun) Vol. 21, No. 3, pp. 153-60.
Journal code: 8000029. ISSN: 0196-0709.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200009

ENTRY DATE: Entered STN: 5 Oct 2000
Last Updated on STN: 5 Oct 2000
Entered Medline: 28 Sep 2000

AB PURPOSE: Platelet-derived growth factor basic 30-kD disulfide-bonded dimer of A and B chains (PDGF-AA, PDGF AB, PDGF-BB) and a cytokine, promoting wound healing by its mitogenicity for fibroblast and by stimulating the production of fibronectin and hyaluronic acid. This article investigates the effect of PDGF on the healing process of tympanic membrane (TM) perforation. MATERIALS AND METHODS: The pars tensa of the posterior aspect of the TM of rats was excised and treated with 2 microg of PDGF-AA or placebo. The animals were killed at 3, 5, 7, 9, 11, 15, and 28 days after operation. The healing process of TM perforation was observed with a telescope and light microscope. The temporal bones were also immunohistochemically examined for PDGF-alpha receptor (PDGF-R(alpha)) and fibronectin. RESULTS: All PDGF-AA-treated TM were completely closed by 5 days after surgery, whereas some of the placebo-treated TM were not closed at 15 postoperative days. PDGF-AA induced the most prominent proliferation of the connective tissue by 9 postoperative days, after which the growth of the connective tissue decreased. By the 4th postoperative week, the PDGF-treated TM were slightly thicker than normal TM. An intense expression of fibronectin was detected in the connective tissue layer of the TM that were treated with PDGF-AA. PDGF-R(alpha) was expressed in the epithelial layer of both the PDGF-treated and control TM. CONCLUSION: These results show that PDGF-AA speeds up the healing process of TM defect, improves the rate of healing, and prevents atrophic changes in the healed TM by promoting the connective tissue growth. The use of PDGF-AA can be an effective alternative to surgery for managing TM perforations.

L6 ANSWER 18 OF 23 MEDLINE on STN
ACCESSION NUMBER: 1999387526 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10459770
TITLE: Novel formulation of fibroblast growth factor-2 in a hyaluronan gel accelerates fracture healing in nonhuman primates.
AUTHOR: Radomsky M L; Aufdemorte T B; Swain L D; Fox W C; Spiro R C; Poser J W
CORPORATE SOURCE: Orquest, Mountain View, California 94043, USA.
SOURCE: Journal of orthopaedic research : official publication of the Orthopaedic Research Society, (1999 Jul) Vol. 17, No. 4, pp. 607-14.
Journal code: 8404726. ISSN: 0736-0266.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199909
ENTRY DATE: Entered STN: 13 Sep 1999
Last Updated on STN: 13 Sep 1999
Entered Medline: 2 Sep 1999

AB Recent advances in understanding the biology of fracture healing and the availability of specific macromolecules has resulted in the development of novel treatments for injuries to bone. Fibroblast growth factor-2 or basic fibroblast growth factor (4 mg/ml), a potent mitogen, and hyaluronan (20 mg/ml), an extracellular matrix component, were combined into a viscous gel formulation intended for direct, percutaneous injection into fresh fractures. In an experimental primate fracture model, a bilateral 1-mm-gap osteotomy was surgically created in the fibulae of baboons. A single direct administration of this hyaluronan/fibroblast growth factor-2 formulation to the defect site significantly promoted local fracture healing as evidenced by increased callus formation and mechanical strength. Radiographic analysis showed

that the callus area was statistically significantly larger at the treated sites than at the untreated sites. Specimens treated with 0.1, 0.25, and 0.75 ml hyaluronan /fibroblast growth factor-2 demonstrated a 48, 50, and 34% greater average load at failure and an 82, 104, and 66% greater energy to failure than the untreated controls, respectively. By histologic analysis, the callus size, periosteal reaction, vascularity, and cellularity were consistently more pronounced in the treated osteotomies than in the untreated controls. These results suggest that hyaluronan/fibroblast growth factor-2 may provide a significant advance in the treatment of fractures.

L6 ANSWER 19 OF 23 MEDLINE on STN
ACCESSION NUMBER: 1999116173 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9917648
TITLE: Potential role of fibroblast growth factor in enhancement of fracture healing.
AUTHOR: Radomsky M L; Thompson A Y; Spiro R C; Poser J W
CORPORATE SOURCE: Orquest Inc., Mountain View, CA 94043-5712, USA.
SOURCE: Clinical orthopaedics and related research, (1998 Oct) No. 355 Suppl, pp. S283-93.
Journal code: 0075674. ISSN: 0009-921X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199902
ENTRY DATE: Entered STN: 23 Feb 1999
Last Updated on STN: 3 Mar 2000
Entered Medline: 10 Feb 1999

AB Fibroblast growth factors are present in significant amounts in bone and several studies have suggested that they may be involved in normal fracture healing. It is well established that fibroblast growth factors have mitogenic and angiogenic activity on mesoderm and neuroectoderm derived cells. Of particular interest as a member of the fibroblast growth factor family, basic fibroblast growth factor stimulates mitogenesis, chemotaxis, differentiation, and angiogenesis. It also plays an important role in the development of vascular, nervous, and skeletal systems, promotes the maintenance and survival of certain tissues, and stimulates wound healing and tissue repair. Animal studies have shown that the direct injection of fibroblast growth factor into fresh fractures stimulates callus formation, which provides mechanical stability to the fracture, accelerates healing, and restores competence. The matrix used to present the fibroblast growth factor at the fracture site plays a critical role in the effectiveness of the treatment. The evaluation of injectable basic fibroblast growth factor in a sodium hyaluronate gel for its effectiveness in stimulating fracture healing is described. When applied directly into a freshly created fracture in the rabbit fibula, a single injection of the basic fibroblast growth factor and hyaluronan results in the stimulation of callus formation, increased bone formation, and earlier restoration of mechanical strength at the fracture site. The hyaluronan gel serves as a reservoir that sequesters the basic fibroblast growth factor at the injection site for the length of time necessary to create an environment conducive to fracture healing. It is concluded that basic fibroblast growth factor and sodium hyaluronate act synergistically to accelerate fracture healing and that the combination is suitable for clinical evaluation as a therapy in fracture treatment.

L6 ANSWER 20 OF 23 MEDLINE on STN
ACCESSION NUMBER: 1998123914 MEDLINE

DOCUMENT NUMBER: PubMed ID: 9462362
TITLE: Insulin-like growth factor I increases bone formation in old or corticosteroid treated rats.
AUTHOR: Prisell P T; Aspenberg P; Wikstrom B; Wredmark T; Norstedt G
CORPORATE SOURCE: Department of Orthopedic Surgery, Novum, Huddinge University Hospital, Sweden.
SOURCE: Acta orthopaedica Scandinavica, (1997 Dec) Vol. 68, No. 6, pp. 586-92.
Journal code: 0370352. ISSN: 0001-6470.
PUB. COUNTRY: Norway
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Space Life Sciences
ENTRY MONTH: 199802
ENTRY DATE: Entered STN: 6 Mar 1998
Last Updated on STN: 6 Mar 1998
Entered Medline: 26 Feb 1998

AB We studied bone induction in subcutaneous implants of demineralized bone matrix with or without insulin-like growth factor I (IGF-I) in aged or corticosteroid-treated rats. Each rat carried one pair of implants, one control and one experiment implant, containing IGF-I dissolved in a hyaluronan solution for slow release. The rats were killed after 3 weeks and the results were evaluated by measuring the calcium content of implants. Young (6-7 weeks) and old (19-27 months) rats were used. A group of young rats was treated for 1 week with subcutaneous injections of 140 micrograms/kg dexamethasone daily. Old rats produced only approximately 1% as much bone as young rats. Local delivery of IGF-I did not increase bone formation in young rats. In old rats, bone formation was increased by IGF-I, 3000 ng/implant. Corticosteroids reduced bone formation in young rats. This effect was partially reversed by local administration of IGF-I.

L6 ANSWER 21 OF 23 MEDLINE on STN
ACCESSION NUMBER: 97422303 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9278071
TITLE: Stimulation of proteoglycan synthesis in explants of porcine articular cartilage by recombinant osteogenic protein-1 (bone morphogenetic protein-7).
AUTHOR: Lietman S A; Yanagishita M; Sampath T K; Reddi A H
CORPORATE SOURCE: Department of Orthopaedic Surgery, The Johns Hopkins University School of Medicine, Baltimore, Maryland 21205, USA.
SOURCE: The Journal of bone and joint surgery. American volume, (1997 Aug) Vol. 79, No. 8, pp. 1132-7.
Journal code: 0014030. ISSN: 0021-9355.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199709
ENTRY DATE: Entered STN: 26 Sep 1997
Last Updated on STN: 26 Sep 1997
Entered Medline: 18 Sep 1997

AB Osteogenic protein-1 (also known as bone morphogenetic protein-7) is a member of the bone morphogenetic protein family. Bone morphogenetic proteins and related members of the TGF-beta (transforming growth factor-beta) superfamily are involved in the development and repair of bone. Recombinant bone morphogenetic proteins induce the formation of new cartilage and bone at heterotopic sites. We investigated the influence of recombinant osteogenic protein-1 (at doses of three, ten, thirty, or 100

nanograms per milliliter) on the synthesis and release of proteoglycans and the maintenance of a steady-state concentration of proteoglycans in explants of porcine articular cartilage that were maintained in chemically defined serum-free medium. We found a dose-dependent stimulation of proteoglycan synthesis and a concurrent decrease in the rate of release of proteoglycans from the explants. The size of the proteoglycan monomers and the composition of the glycosaminoglycan chains in the untreated articular cartilage were similar to those in the articular cartilage treated with osteogenic protein-1. The capacity of the newly synthesized proteoglycan monomers to form aggregates with exogenous hyaluronic acid was found to be similar to that of proteoglycans in bovine nasal cartilage. Our results demonstrated that osteogenic protein-1 stimulated the synthesis of proteoglycans and diminished the release of proteoglycans from explants of porcine articular cartilage. CLINICAL RELEVANCE: The maintenance and repair of articular cartilage is a formidable challenge in clinical orthopaedics. The stimulation of proteoglycan synthesis by osteogenic protein-1 (bone morphogenetic protein-7) in explants of cartilage maintained in chemically defined serum-free medium implies that recombinant osteogenic protein-1 may play a role in the maintenance of a steady-state concentration of proteoglycans in articular cartilage, a desirable prerequisite for optimum repair of cartilage. Osteogenic protein-1 can initiate the formation of cartilage from mesenchymal cells. Once new cartilage has formed at the site of repair, osteogenic protein-1 also may maintain the synthesis of proteoglycans.

L6 ANSWER 22 OF 23 MEDLINE on STN
ACCESSION NUMBER: 96218876 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8648512
TITLE: Basic fibroblast growth factor enhances bone-graft incorporation: dose and time dependence in rats.
AUTHOR: Wang J S; Aspenberg P
CORPORATE SOURCE: Department of Orthopedics, Lund University Hospital, Sweden.
SOURCE: Journal of orthopaedic research : official publication of the Orthopaedic Research Society, (1996 Mar) Vol. 14, No. 2, pp. 316-23.
Journal code: 8404726. ISSN: 0736-0266.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199607
ENTRY DATE: Entered STN: 5 Aug 1996
Last Updated on STN: 5 Aug 1996
Entered Medline: 25 Jul 1996

AB In a previous study, we found that basic fibroblast growth factor could stimulate bone-graft incorporation. In the present study, the effects of different doses and implantation times were further studied, using the bone conduction chamber, in rats. Inside the chamber, the graft is isolated from the surrounding tissues except at one end, where small openings embedded in host bone allow ingrowth of tissue. The distance that new tissues had reached from the openings into the graft was measured on histological slides. Bone grafts were obtained from the proximal tibiae of donor rats, frozen at -70 degrees C, and lipid-extracted. Before implantation, they were soaked overnight in a hyaluronate gel with or without basic fibroblast growth factor and then were fitted into the chambers, which were implanted in the proximal tibiae of recipient rats. In a dose-response experiment, grafts containing 0.3, 8, 40, 200, or 1,000 ng of basic fibroblast growth factor were compared with grafts treated with carrier gel only, after an implantation time of 6 weeks. Fibrous tissue always penetrated the grafts further than the ingrown bone; the distance that it reached from the ingrowth

openings (total ingrowth distance) was increased by all of the doses except 0.3 ng per implant. The distance of bone ingrowth was increased by 8, 40, and 200 ng. The increased total ingrowth with 1,000 ng was due to an increased amount of fibrous tissue ahead of the bone, whereas with the lower doses the increase was due to more bone. Thus, the dose had an effect on the type of ingrown tissue found in the graft. In a time-effect study, grafts treated with 40 ng of basic fibroblast growth factor had a higher uptake of [99mTc]MDP at 2 and 4 weeks and an increased bone ingrowth distance at 10 weeks. The radioactivity from [125I]basic fibroblast growth factor declined with a half-life of 17 hours. The results suggest that basic fibroblast growth factor may be beneficial for the incorporation of contained bone grafts; studies using more clinically relevant models are required.

L6 ANSWER 23 OF 23 MEDLINE on STN
ACCESSION NUMBER: 94361507 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8080268
TITLE: Transforming growth factor-beta stimulates retinoic acid-induced proteoglycan depletion in intact articular cartilage.
AUTHOR: Von den Hoff H W; de Koning M H; van Kampen G P; van der Korst J K
CORPORATE SOURCE: Jan van Breemen Instituut, Center for Rheumatology and Rehabilitation, Amsterdam, The Netherlands.
SOURCE: Archives of biochemistry and biophysics, (1994 Sep) Vol. 313, No. 2, pp. 241-7.
Journal code: 0372430. ISSN: 0003-9861.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199409
ENTRY DATE: Entered STN: 13 Oct 1994
Last Updated on STN: 13 Oct 1994
Entered Medline: 30 Sep 1994

AB Cartilage-bearing sesamoid bones from the metacarpophalangeal joints of adult cows were cultured with retinoic acid for 1 week and allowed to recover in control medium for another 2 weeks. Retinoic acid decreased the proteoglycan synthesis of the cartilage to 33% of control values, and induced 26% loss of proteoglycans from the matrix. During recovery, the synthesis of proteoglycans returned to the control level but their content remained reduced. Transforming growth factor-beta (TGF-beta 1, 5 ng/ml) was added to the culture medium to stimulate the recovery. However, TGF-beta depressed the synthesis of proteoglycans and increased their loss to 61%. Only the large aggregating species, aggrecan, was lost from the matrix. The half-life of proteoglycans synthesized during recovery in control medium was 12.7 days, which was reduced to 8.7 days by TGF-beta. The proteoglycan half-life in control cartilage cultured without retinoic acid or TGF-beta was 33.8 days. Neither retinoic acid nor TGF-beta-induced changes in the hyaluronate content of the tissue. Aggrecans and small proteoglycans synthesized in the presence of TGF-beta were larger than those in controls. The synthesis of the small proteoglycans was stimulated 4.5-fold by TGF-beta, and their content was increased. The results show that TGF-beta can stimulate depletion of aggrecan in retinoic acid-treated cartilage. This indicates a catabolic function of TGF-beta in cartilage remodeling.

L6 ANSWER 1 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:521606 CAPLUS
DOCUMENT NUMBER: 144:495201
TITLE: Porous gelatin-chondroitin-hyaluronate tri-copolymer scaffold containing microspheres loaded with TGF-β1 induces differentiation of mesenchymal stem cells in vivo for enhancing cartilage repair
AUTHOR(S): Fan, Hongbin; Hu, Yunyu; Qin, Ling; Li, Xusheng; Wu, Hong; Lv, Rong
CORPORATE SOURCE: Institute of Orthopaedics and Traumatology, Xijing Hospital, The Fourth Military Medical University, Xi'an, Peop. Rep. China
SOURCE: Journal of Biomedical Materials Research, Part A (2006), 77A(4), 785-794
CODEN: JBMRCH; ISSN: 1549-3296
PUBLISHER: John Wiley & Sons, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The aim of the study was to produce a novel porous gelatin-chondroitin-hyaluronate scaffold in combination with a controlled release of transforming growth factor β1 (TGF-β1), which induced the differentiation of mesenchymal stem cells (MSCs) in vivo for enhancing cartilage repair. Gelatin microspheres loaded with TGF-β1 (MS-TGFβ1) showed a fast release at the initial phase (37.4%), and the ultimate accumulated release was 83.1% by day 18. The autologous MSCs seeded on MS-TGFβ1/scaffold were implanted to repair full-thickness cartilage defects in rabbits as in vivo differentiation repair group, while MSCs differentiated in vitro were seeded on scaffold without MS-TGFβ1 to repair the contralateral cartilage defects (n = 30). Fifteen addnl. rabbits without treatment for defects were used as control. Histol. observation showed that the in vivo differentiation repair group had better chondrocyte morphol., integration, continuous subchondral bone, and much thicker newly formed cartilage layer when compared to in vitro differentiation repair group 12 and 24 wk, postoperatively. There was a significant difference in histol. grading score between these 2 exptl. groups, and both showed much better repair than that of the control. The present study implied that the novel scaffold with MS-TGFβ1 might serve as a new way to induce the differentiation of MSCs in vivo to enhance the cartilage repair.
REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:37177 CAPLUS
DOCUMENT NUMBER: 144:135230
TITLE: Pharmaceutical composition comprising FGF18 and IL-1 antagonist and method of use
INVENTOR(S): Moore, Emma E.; Ellsworth, Jeff L.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 14 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006009389	A1	20060112	US 2005-175734	20050706
WO 2006014444	A1	20060209	WO 2005-US23866	20050706

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ,

LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA,
NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,
SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU,
ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2004-585655P P 20040706

AB Fibroblast growth factor 18 (FGF18) is known to stimulate the proliferation of chondrocytes, bone, and nervous tissue, resulting in repair of diseased tissue. When an interleukin-1 (IL-1) antagonist is administered in addition to FGF18, the effects on the IL-1 mediated disease and also, the effect on cartilage, bone, and nervous cell proliferation, are found to be greater than administration of FGF18 or the IL-1 antagonist alone. The present invention encompasses a pharmaceutical composition that combines FGF18 with IL-1 antagonist and methods of treating IL-1 mediated disease using this pharmaceutical composition Thus, a combination of FGF18 and IL-1 antagonist, with and without hyaluronan carrier as intraarticular injection was used for the treatment of rheumatoid arthritis in rat models.

L6 ANSWER 3 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:902008 CAPLUS
DOCUMENT NUMBER: 143:235567
TITLE: Use of a specific mixture of polysaccharides, named by the inventor Ezbone, containing hyaluronic acid, chondroitin-6 sulfates, dermatan sulfates and heparin, in bone cicatrization
INVENTOR(S): Zanchetta, Philippe
PATENT ASSIGNEE(S): Fr.
SOURCE: Fr. Demande, 15 pp.
CODEN: FRXXBL
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2866571	A1	20050826	FR 2004-1700	20040220

PRIORITY APPLN. INFO.: FR 2004-1700 20040220

AB The invention composition helps the healing of the bone. The composition contains 49% hyaluronic acid in the form of sodium salt, 49% chondroitin-6 sulfate, and 2% chondroitin-B sulfate (dermatan sulfate). The whole composition forms a homogeneous gel by the addition of 2.5 mL of 9% sodium chloride solution and can also contain 25000 IU heparin. The mixture of polysaccharides used in the invention can be also presented in a hydrated form, such as a membrane, or a three-dimensional alveolate solid structure. The mixture of polysaccharides defined above can be used for the preparation of a coating for bone implant, an osteoconductive filling material, or any invasive surgical material which can be thus integrated very quickly in the bone. A hormone or a growth factor, in particular BMP can also be added to the mixture Association of the mixture of polysaccharides to a osteoinductive material would increase the speed of the cicatrization. This invention is particularly advantageous to treat noncrit. bone lesions, to accelerate the cicatrization of bone fractures and to obtain spinal fusion. Efficacy of the above formulation in cicatrization of rats bone is shown.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:528534 CAPLUS
DOCUMENT NUMBER: 140:187234
TITLE: Repair of reconstituted freeze-dried bone allograft to segmental radius defects in rabbits
AUTHOR(S): Chen, Qing; Gu, Jiefu; Cai, Lin; Gan, Yu
CORPORATE SOURCE: Zhongnan Hospital, Wuhan University, Wuhan, 430071, Peop. Rep. China
SOURCE: Wuhan Daxue Xuebao, Yixueban (2002), 23(3), 251-254
CODEN: WDXYAA
PUBLISHER: Wuhan Daxue Xuebao, Yixueban Faxingbu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB The effect of basic fibroblast growth factor (bFGF) and hyaluronic acid gel (HAG) combined with freeze-dried bone allograft in repairing radius defects was investigated and their mechanism was explored. Fifteen mm segmental bone /periosteum defects were created in 36 New Zealand rabbits on bilateral radius and were treated with three different kinds of implants: A, bFGF and HAG combined with freeze-dried bone; B, bFGF combined with freeze-dried bone; C, a single freeze-dried bone as control. The repairs of defects were observed by radiol. and histol. method and analyzed by radionuclide bone imaging, and calcium contents were detected at different periods. The new bone formation, bone metabolic activity and calcium contents of defects in Group A were higher than that in Group B, and the data of Group B were higher than that in Group C. The defects of Group A were healed at the 8th week, and those of Group B were healed at the 10th week. As an osteogenetic factor, bFGF promotes the new bone formation. As a slow-release carrier, HAG enhances the effectiveness of bFGF. The combination of bFGF, HAG and freeze-dried bone allograft can repair the defects more effectively.

L6 ANSWER 5 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:872870 CAPLUS
DOCUMENT NUMBER: 136:339321
TITLE: Anti-inflammatory and chondroprotective effect of TSG-6 (tumor necrosis factor-α-stimulated gene-6) in murine models of experimental arthritis
AUTHOR(S): Bardos, Tamas; Kamath, Rajesh V.; Mikecz, Katalin; Glant, Tibor T.
CORPORATE SOURCE: Departments of Orthopedic Surgery, Rush University, Chicago, IL, 60612, USA
SOURCE: American Journal of Pathology (2001), 159(5), 1711-1721
CODEN: AJPAA4; ISSN: 0002-9440
PUBLISHER: American Society for Investigative Pathology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Tumor necrosis factor-α (TNF-α)-stimulated gene-6 (TSG-6) is up-regulated by various cytokines and growth factors. TSG-6 binds to hyaluronan in inflamed synovial tissue and forms a complex with a serine protease inter-α-trypsin inhibitor (IαI), increasing the protease inhibitory effect of IαI >100-fold. The TSG-6/IαI complex then blocks serine proteases, including the plasminogen-plasmin activation, probably the most important component in the activation processes of matrix metalloproteinases. To gain insight into the mechanisms of TSG-6 action in arthritis, the authors have used an autoimmune murine model (proteoglycan-induced arthritis) for systemic, and a monoarticular form of arthritis (antigen-induced arthritis) for local treatment of arthritis with recombinant mouse TSG-6 (rmTSG-6). I.v. injection of rmTSG-6 induced a dramatic reduction of edema in acutely inflamed joints by immobilizing CD44-bound

hyaluronan and, in long-term treatment, protected cartilage from degradation and blocked subchondral and periosteal bone erosion in inflamed joints. The intra-articular injection of a single dose (100 μg) of rmTSG-6 exhibited a strong chondroprotective effect for up to 5-7 days, preventing cartilage proteoglycan from metalloproteinase-induced degradation In contrast, rmTSG-6 did not postpone the onset, nor reduce the incidence of arthritis. The authors were unable to detect any differences between control and rmTSG-6-treated animals when various serum markers (including pro- and anti-inflammatory cytokines, auto- and heteroantibody productions) or antigen-specific T-cell responses were compared, nor when the expressions of numerous cell surface receptors or adhesion mols. were measured. TSG-6 seems to play a critical neg. regulatory feed-back function in inflammation, especially in arthritic processes.

REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:909060 CAPLUS
DOCUMENT NUMBER: 134:61583
TITLE: Collagen matrix and growth factors in non-immunogenic compositions for programming an organic matrix for remodeling into a target tissue
INVENTOR(S): Ashkar, Samy; Atala, Anthony
PATENT ASSIGNEE(S): Children's Medical Center Corp., USA
SOURCE: U.S., 10 pp., Cont.-in-part of U. S. Ser. No. 937,873.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6165487	A	20001226	US 1998-58048	19980409
WO 9814222	A1	19980409	WO 1997-US17530	19970929
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
WO 9952572	A1	19991021	WO 1999-US7742	19990408
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9933875	A1	19991101	AU 1999-33875	19990408
PRIORITY APPLN. INFO.:			US 1996-27123P	P 19960930
			US 1997-937873	A2 19970929
			WO 1997-US17530	A1 19970929
			US 1998-58048	A 19980409
			WO 1999-US7742	W 19990408

AB Methods for programming a non-immunogenic matrix for remodeling into a target tissue are disclosed. Also disclosed are compns. containing demineralized collagen and a growth factor, e.g., osteopontin, which can promote the growth of selected tissue types in a

subject. Methods for preparing the compns. are also described. The methods and compns. are useful for treatment of defects in tissues such as bone, cartilage, and muscle. For example, a bone -forming matrix was prepared by suspending demineralized bone in a physiol. saline solution with 0.1% osteopontin, 0.01% bone sialoprotein, and 0.1% of high-mol.-weight hyaluronic acid and drying. The bone-forming matrix provided new bone formation in bone defects. It is believed that the bone forming compns. of the invention provided results equal to, or superior to, the results seen with bone allograft treatment.

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 7 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:405465 CAPLUS

DOCUMENT NUMBER: 133:145429

TITLE: Effects of platelet-derived growth factor-AA on the healing process of tympanic membrane perforation

AUTHOR(S): Yeo, Sang W.; Kim, Soo-Whan; Suh, Byung-Do; Cho, Seung-Ho

CORPORATE SOURCE: Department of Otolaryngology-Head and Neck Surgery, College of Medicine, The Catholic University of Korea, Seoul, 137-040, S. Korea

SOURCE: American Journal of Otolaryngology (2000), 21(3), 153-160
CODEN: AJOTDP; ISSN: 0196-0709

PUBLISHER: W. B. Saunders Co.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Purpose: Platelet-derived growth factor basic 30 kDa disulfide-bonded dimer of A and B chains (PDGF-AA, PDGF AB, PDGF-BB) and a cytokine, promoting wound healing by its mitogenicity for fibroblast and by stimulating the production of fibronectin and hyaluronic acid. This article investigates the effect of PDGF on the healing process of tympanic membrane (TM) perforation. Materials and Methods: The pars tensa of the posterior aspect of the TM of rats was excised and treated with 2 μg of PDGF-AA or placebo. The animals were killed at 3, 5, 7, 9, 11, 15, and 28 days after operation. The healing process of TM perforation was observed with a telescope and light microscope. The temporal bones were also immunohistochem. examined for PDGF-α receptor (PDGF-Rα) and fibronectin. Results: All PDGF-AA- treated TM were completely closed by 5 days after surgery, whereas some of the placebo-treated TM were not closed at 15 postoperative days. PDGF-AA induced the most prominent proliferation of the connective tissue by 9 postoperative days, after which the growth of the connective tissue decreased. By the 4th postoperative week, the PDGF-treated TM were slightly thicker than normal TM. An intense expression of fibronectin was detected in the connective tissue layer of the TM that were treated with PDGF-AA. PDGF-Rα was expressed in the epithelial layer of both the PDGF-treated and control TM. Conclusion: These results show that PDGF-AA speeds up the healing process of TM defect, improves the rate of healing, and prevents atrophic changes in the healed TM by promoting the connective tissue growth. The use of PDGF-AA can be an effective alternative to surgery for managing TM perforations.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 8 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:587085 CAPLUS

DOCUMENT NUMBER: 132:580

TITLE: Novel formulation of fibroblast growth factor-2 in a hyaluronan gel accelerates fracture healing in nonhuman primates

AUTHOR(S): Radomsky, Michael L.; Aufdemorte, Thomas B.; Swain, Larry D.; Fox, W. Casey; Spiro, Robert C.; Poser, James W.
CORPORATE SOURCE: Orquest, Mountain View, CA, 94043, USA
SOURCE: Journal of Orthopaedic Research (1999), 17(4), 607-614
CODEN: JOREDR; ISSN: 0736-0266
PUBLISHER: Journal of Bone and Joint Surgery, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Recent advances in understanding the biol. of fracture healing and the availability of specific macromols. has resulted in the development of novel treatments for injuries to bone. Fibroblast growth factor-2 or basic fibroblast growth factor (4 mg/mL), a potent mitogen, and hyaluronan (20 mg/mL), an extracellular matrix component, were combined into a viscous gel formulation intended for direct, percutaneous injection into fresh fractures. In an exptl. primate fracture model, a bilateral 1-mm-gap osteotomy was surgically created in the fibulae of baboons. A single direct administration of this hyaluronan/fibroblast growth factor-2 formulation to the defect site significantly promoted local fracture healing as evidenced by increased callus formation and mech. strength. Radiog. anal. showed that the callus area was statistically significantly larger at the treated sites than at the untreated sites. Specimens treated with 0.1, 0.25, and 0.75 mL hyaluronan/fibroblast growth factor-2 demonstrated a 48, 50, and 34% greater average load at failure and an 82, 104, and 66% greater energy to failure than the untreated controls, resp. By histol. anal., the callus size, periosteal reaction, vascularity, and cellularity were consistently more pronounced in the treated osteotomies than in the untreated controls. These results suggest that hyaluronan/fibroblast growth factor-2 may provide a significant advance in the treatment of fractures.

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 9 OF 23 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:617981 CAPLUS
DOCUMENT NUMBER: 127:253211
TITLE: Method of promoting bone growth with hyaluronic acid and growth factors
INVENTOR(S): Radomsky, Michael
PATENT ASSIGNEE(S): Orquest, Inc., USA
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9732591	A1	19970912	WO 1997-US4810	19970305
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, YU				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2246747	AA	19970912	CA 1997-2246747	19970305
AU 9725449	A1	19970922	AU 1997-25449	19970305
AU 729086	B2	20010125		
CN 1212628	A	19990331	CN 1997-192822	19970305

EP 910389	A1	19990428	EP 1997-916976		19970305
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
NZ 331238	A	20000526	NZ 1997-331238		19970305
JP 2002504083	T2	20020205	JP 1997-532070		19970305
PRIORITY APPLN. INFO.:			US 1996-611690	A	19960305
			US 1997-811971	A	19970305
			WO 1997-US4810	W	19970305

AB A bone growth-promoting composition is provided comprising hyaluronic acid and a growth factor. The composition has a viscosity and biodegradability sufficient to persist at the site of desired bone growth for a period of time sufficient to promote the bone growth. Preferably hyaluronic acid is used in a composition range of 0.1 to 4 % and preferred growth factor is bFGF, present in a concentration range of 10-6 to 100 mg/mL. An aqueous solution containing Na hyaluronate, bFGF, and Na citrate was injected with a needle between the periosteum and parietal bone of rats. The animals were euthanized 14 days following treatment and new bone formation was evaluated.

L7 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:37177 CAPLUS
DOCUMENT NUMBER: 144:135230
TITLE: Pharmaceutical composition comprising FGF18 and IL-1 antagonist and method of use
INVENTOR(S): Moore, Emma E.; Ellsworth, Jeff L.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 14 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006009389	A1	20060112	US 2005-175734	20050706
WO 2006014444	A1	20060209	WO 2005-US23866	20050706

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2004-585655P P 20040706

AB Fibroblast growth factor 18 (FGF18) is known to stimulate the proliferation of chondrocytes, bone, and nervous tissue, resulting in repair of diseased tissue. When an interleukin-1 (IL-1) antagonist is administered in addition to FGF18, the effects on the IL-1 mediated disease and also, the effect on cartilage, bone, and nervous cell proliferation, are found to be greater than administration of FGF18 or the IL-1 antagonist alone. The present invention encompasses a pharmaceutical composition that combines FGF18 with IL-1 antagonist and methods of treating IL-1 mediated disease using this pharmaceutical composition Thus, a combination of FGF18 and IL-1 antagonist, with and without hyaluronan carrier as intraarticular injection was used for the treatment of rheumatoid arthritis in rat models.

L7 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:696705 CAPLUS
DOCUMENT NUMBER: 143:179619
TITLE: Drug delivery to a joint comprising a polymeric or non-polymeric carrier
INVENTOR(S): Hotchkiss, Robert N.; Koski, John A.
PATENT ASSIGNEE(S): Orthobiologica, Inc., USA
SOURCE: PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005070333	A1	20050804	WO 2005-US999	20050113

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,

GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,
RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
MR, NE, SN, TD, TG

US 2005152949 A1 20050714 US 2005-35375 20050113
PRIORITY APPLN. INFO.: US 2004-536135P P 20040113
US 2004-566737P P 20040429

AB A method of intra-articular drug delivery may include selecting an attachment zone in a synovial joint and affixing a drug release device in the attachment zone. The drug release device comprises a base affixable in the attachment zone, a sustained-release drug carrier, and a drug. The device is positioned so that it releases the drug into the synovial fluid of the synovial joint, and so that agitation of the synovial fluid facilitates elution of the drug from the drug release device. For example, a sustained-release device included a polymeric matrix or liposome from which drug was released by diffusion and/or degradation of the matrix. The release pattern is usually principally determined by the matrix material, as well as by the percent loading, method of manufacture, type of drug being administered and type of device, for example, microsphere. A major advantage of a biodegradable controlled release system over others was that it did not require the surgical removal of the drug depleted device, which was slowly degraded and absorbed by the patient's body, and ultimately cleared along with other soluble metabolic waste products. Sustained-release compns. include poly(glycolic acid), poly(lactic acid), polyester, collagen, a hydrogel, and hyaluronic acid. Exemplary therapeutic agents include bupivacaine, lidocaine, dexamethasone, a nonsteroidal antiinflammatory agent, an antibiotic, an immunomodulator, a bone morphogenic protein, a cytokine, a growth factor, and a vascular endothelial growth factor.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:602452 CAPLUS
DOCUMENT NUMBER: 131:341857
TITLE: New strategy for chemical modification of hyaluronic acid: preparation of functionalized derivatives and their use in the formation of novel biocompatible hydrogels
AUTHOR(S): Bulpitt, Paul; Aeschlimann, Daniel
CORPORATE SOURCE: Division of Orthopedic Surgery, H5/301 Clinical Science Center, University of Wisconsin, Madison, WI, 53792, USA
SOURCE: Journal of Biomedical Materials Research (1999), 47(2), 152-169
CODEN: JBMRBG; ISSN: 0021-9304
PUBLISHER: John Wiley & Sons, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Biodegradable materials for spatially and temporally controlled delivery of bioactive agents such as drugs, growth factors, or cytokines are key to facilitating tissue repair. We have developed a versatile method for chemical crosslinking high-mol.-weight hyaluronic acid under physiol. conditions yielding biocompatible and biodegradable hydrogels. The method is based on the introduction of functional groups onto hyaluronic acid by formation of an active ester at the carboxylate of the glucuronic acid moiety and subsequent substitution with a side chain containing a nucleophilic group on one end and a (protected) functional group on the other. We have formed hyaluronic acid with amino or aldehyde functionality, and subsequently hydrogels with these hyaluronic acid derivs. and bifunctional crosslinkers or mixts. of the hyaluronic acid derivs. carrying different functionalities using active ester- or aldehyde-mediated reactions. Size anal. of the hyaluronic acid derivs. showed that the chemical modification did not lead to fragmentation of the polysaccharide. Hydrogels formed with hyaluronic acid derivatized to a varying degree and crosslinked with low- or high-mol.-weight crosslinkers were evaluated for biodegradability by digestion with hyaluronidase and for biocompatibility and ectopic bone formation by s.c. implantation in rats. Several hydrogel formulations showed excellent cell infiltration and chondro-osseous differentiation when loaded with bone morphogenetic protein-2 (BMP-2). Synergistic action of insulin-like growth factor-1 with BMP-2 promoted cartilage formation in this model, while addition of transforming growth factor-β and BMP-2 led to rapid replacement of the matrix by bone.
REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:700264 CAPLUS
DOCUMENT NUMBER: 128:12477
TITLE: Adhesion and migration are differentially regulated in hematopoietic progenitor cells by cytokines and extracellular matrix
AUTHOR(S): Strobel, Eva-Susanne; Mobest, Dieter; von Kleist, Sabine; Dangel, Matthias; Ries, Stefan; Mertelsmann, Roland; Henschler, Reinhard
CORPORATE SOURCE: Experimental Hematology Group, Department of Hematology and Oncology, University Medical Center, Freiburg, Germany
SOURCE: Blood (1997), 90(9), 3524-3532
CODEN: BLOOAW; ISSN: 0006-4971
PUBLISHER: Saunders
DOCUMENT TYPE: Journal

LANGUAGE: English

AB The conditions that control the migratory status of hematopoietic progenitor cells on extracellular matrix (ECM) and that decide whether a cell migrates or adheres are incompletely understood. The authors analyzed the migratory behavior of murine hematopoietic progenitor cells factor-dependent-cell-paterson (FDCP)-mix and purified lin-Sca1+ bone marrow cells on ECM. They found that migration on fibronectin (Fn) or laminin (Lam) becomes dependent on β1-integrins if a surface restraint force is introduced by tilting the ECM-coated culture vessels. Under these conditions, migration specifically occurred on Fn and Lam, and was not detected on collagen IV-, hyaluronate -, or bovine serum albumin- coated surfaces. Migration depended on the continuous presence of hematopoietic cytokines interleukin-3 (IL-3), granulocyte colony-stimulating factor (G-CSF), macrophage-CSF (M-CSF), granulocyte-macrophage-CSF (GM-CSF), or stem cell factor (SCF), whereas other cytokines, such as IL-8, macrophage inflammatory protein -1α, macrophage-chemotactic and activating factor, and erythropoietin resulted in very little or no migratory response. IL-3 induced migration was synergistically enhanced by other CSFs, but was completely inhibited by addition of transforming growth factor -β1. In contrast to firm local adhesion of previously cytokine depleted progenitors that was rapidly inducible within 1 h after exposure to cytokines, preincubation on Fn matrix for 4 to 6 h was required before cytokines could induce migration. A sudden increase of cytokine concentration reversibly inhibited migration and induced a fully adhesive state; this effect could be prolonged by consecutive stimulation with heterologous cytokines. Whereas cytokines activated resting progenitor cells to migrate on ECM, cell migration speed was regulated by Fn concentration These results indicate that β1-integrin-mediated progenitor cell adhesion and migration are differentially regulated by external stimuli and suggest that this regulation corresponds to different activation states of β1-integrins in hematopoietic progenitor cells.

L9 ANSWER 3 OF 5 MEDLINE on STN

ACCESSION NUMBER: 1999380243 MEDLINE

DOCUMENT NUMBER: PubMed ID: 10449626

TITLE: New strategy for chemical modification of hyaluronic acid: preparation of functionalized derivatives and their use in the formation of novel biocompatible hydrogels.

AUTHOR: Bulpitt P; Aeschlimann D

CORPORATE SOURCE: Division of Orthopedic Surgery, University of Wisconsin, H5/301 Clinical Science Center, 600 Highland Avenue, Madison, Wisconsin 53792, USA.

SOURCE: Journal of biomedical materials research, (1999 Nov) Vol. 47, No. 2, pp. 152-69.
Journal code: 0112726. ISSN: 0021-9304.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199909

ENTRY DATE: Entered STN: 12 Oct 1999
Last Updated on STN: 12 Oct 1999
Entered Medline: 28 Sep 1999

AB Biodegradable materials for spatially and temporally controlled delivery of bioactive agents such as drugs, growth factors, or cytokines are key to facilitating tissue repair. We have developed a versatile method for chemical crosslinking high-molecular-weight hyaluronic acid under physiological conditions yielding biocompatible and biodegradable hydrogels. The method is based on the introduction of functional groups onto hyaluronic acid by formation of an active ester at the carboxylate of the glucuronic acid moiety and subsequent substitution with a side chain containing a nucleophilic group on one end and a (protected) functional group on the

other. We have formed hyaluronic acid with amino or aldehyde functionality, and subsequently hydrogels with these hyaluronic acid derivatives and bifunctional crosslinkers or mixtures of the hyaluronic acid derivatives carrying different functionalities using active ester- or aldehyde-mediated reactions. Size analysis of the hyaluronic acid derivatives showed that the chemical modification did not lead to fragmentation of the polysaccharide. Hydrogels formed with hyaluronic acid derivatized to a varying degree and crosslinked with low- or high-molecular-weight crosslinkers were evaluated for biodegradability by digestion with hyaluronidase and for biocompatibility and ectopic bone formation by subcutaneous implantation in rats. Several hydrogel formulations showed excellent cell infiltration and chondro-osseous differentiation when loaded with bone morphogenetic protein-2 (BMP-2). Synergistic action of insulin-like growth factor-1 with BMP-2 promoted cartilage formation in this model, while addition of transforming growth factor-beta and BMP-2 led to rapid replacement of the matrix by bone.

L9 ANSWER 4 OF 5 MEDLINE on STN
ACCESSION NUMBER: 1999116173 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9917648
TITLE: Potential role of fibroblast growth factor in enhancement of fracture healing.
AUTHOR: Radomsky M L; Thompson A Y; Spiro R C; Poser J W
CORPORATE SOURCE: Orquest Inc., Mountain View, CA 94043-5712, USA.
SOURCE: Clinical orthopaedics and related research, (1998 Oct) No. 355 Suppl, pp. S283-93.
Journal code: 0075674. ISSN: 0009-921X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199902
ENTRY DATE: Entered STN: 23 Feb 1999
Last Updated on STN: 3 Mar 2000
Entered Medline: 10 Feb 1999

AB Fibroblast growth factors are present in significant amounts in bone and several studies have suggested that they may be involved in normal fracture healing. It is well established that fibroblast growth factors have mitogenic and angiogenic activity on mesoderm and neuroectoderm derived cells. Of particular interest as a member of the fibroblast growth factor family, basic fibroblast growth factor stimulates mitogenesis, chemotaxis, differentiation, and angiogenesis. It also plays an important role in the development of vascular, nervous, and skeletal systems, promotes the maintenance and survival of certain tissues, and stimulates wound healing and tissue repair. Animal studies have shown that the direct injection of fibroblast growth factor into fresh fractures stimulates callus formation, which provides mechanical stability to the fracture, accelerates healing, and restores competence. The matrix used to present the fibroblast growth factor at the fracture site plays a critical role in the effectiveness of the treatment. The evaluation of injectable basic fibroblast growth factor in a sodium hyaluronate gel for its effectiveness in stimulating fracture healing is described. When applied directly into a freshly created fracture in the rabbit fibula, a single injection of the basic fibroblast growth factor and hyaluronan results in the stimulation of callus formation, increased bone formation, and earlier restoration of mechanical strength at the fracture site. The hyaluronan gel serves as a reservoir that sequesters the basic fibroblast growth factor at the injection site for the

length of time necessary to create an environment conducive to fracture healing. It is concluded that basic fibroblast growth factor and sodium hyaluronate act synergistically to accelerate fracture healing and that the combination is suitable for clinical evaluation as a therapy in fracture treatment.

L9 ANSWER 5 OF 5 MEDLINE on STN
ACCESSION NUMBER: 1998008117 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9345036
TITLE: Adhesion and migration are differentially regulated in hematopoietic progenitor cells by cytokines and extracellular matrix.
AUTHOR: Strobel E S; Mobest D; von Kleist S; Dangel M; Ries S; Mertelsmann R; Henschler R
CORPORATE SOURCE: Experimental Hematology Group, Department of Hematology and Oncology, University Medical Center, Freiburg, Germany.
SOURCE: Blood, (1997 Nov 1) Vol. 90, No. 9, pp. 3524-32. Journal code: 7603509. ISSN: 0006-4971.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199711
ENTRY DATE: Entered STN: 24 Dec 1997
Last Updated on STN: 24 Dec 1997
Entered Medline: 18 Nov 1997

AB The conditions that control the migratory status of hematopoietic progenitor cells on extracellular matrix (ECM) and that decide whether a cell migrates or adheres are incompletely understood. We analyzed the migratory behavior of murine hematopoietic progenitor cells factor-dependent-cell-paterson (FDCP)-mix and purified lin-Sca1+ bone marrow cells on ECM. We found that migration on fibronectin (Fn) or laminin (Lam) becomes dependent on beta1-integrins if a surface restraint force is introduced by tilting the ECM-coated culture vessels. Under these conditions, migration specifically occured on Fn and Lam, and was not detected on collagen IV-, hyaluronate-, or bovine serum albumin- coated surfaces. Migration depended on the continuous presence of hematopoietic cytokines interleukin-3 (IL-3), granulocyte colony-stimulating factor (G-CSF), macrophage-CSF (M-CSF), granulocyte-macrophage-CSF (GM-CSF), or stem cell factor (SCF), whereas other cytokines, such as IL-8, macrophage inflammatory protein-1alpha, macrophage-chemotactic and activating factor, and erythropoietin resulted in very little or no migratory response. IL-3 induced migration was synergistically enhanced by other CSFs, but was completely inhibited by addition of transforming growth factor -beta1. In contrast to firm local adhesion of previously cytokine depleted progenitors that was rapidly inducible within 1 hour after exposure to cytokines, preincubation on Fn matrix for 4 to 6 hours was required before cytokines could induce migration. A sudden increase of cytokine concentration reversibly inhibited migration and induced a fully adhesive state; this effect could be prolonged by consecutive stimulation with heterologous cytokines. Whereas cytokines activated resting progenitor cells to migrate on ECM, cell migration speed was regulated by Fn concentration. These results indicate that beta1-integrin-mediated progenitor cell adhesion and migration are differentially regulated by external stimuli and suggest that this regulation corresponds to different activation states of beta1-integrins in hematopoietic progenitor cells.

L10 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:12589 CAPLUS
DOCUMENT NUMBER: 134:76442
TITLE: Compositions containing growth factors and methods for forming and strengthening bone
INVENTOR(S): Marchosky, J. Alexander
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001000792	A1	20010104	WO 2000-US17955	20000629
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2377435	AA	20010104	CA 2000-2377435	20000629
US 6372257	B1	20020416	US 2000-606768	20000629
EP 1203074	A1	20020508	EP 2000-943309	20000629
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
AU 782394	B2	20050721	AU 2000-57799	20000629
PRIORITY APPLN. INFO.:			US 1999-141386P P	19990629
			WO 2000-US17955 W	20000629

AB Compns. for stimulating bone growth comprise (a) growth factors, (b) demineralized, non-decalcified bone matrix, (c) a scaffolding material selected from cancelous bone, chitosan, chitosan-protein, and chitosan-protein fibers, and (d) a gel material selected from chitosan and its derivs., alginate, or hyaluronic acid. Addnl., compns. may contain angiogenesis-stimulating materials and osteoinductive materials. Methods for utilizing the compns. for filling in bone defects, promoting rapid fusion of bone fractures, grafts, and bone-prostheses, and promoting strengthening of osteoporotic bones are also provided. For example, bone formation at the site of bone defect was observed 12 wk after the application of the composition containing demineralized bone matrix, hyaluronic acid, and vascular endothelial growth factor.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:1004987 CAPLUS
DOCUMENT NUMBER: 140:8882
TITLE: Composition for filling bone defects based on demineralized lyophilized allograft bone particles in hyaluronate carrier
INVENTOR(S): Gertzman, Arthur A.; Sunwoo, Moon Hae
PATENT ASSIGNEE(S): Musculoskeletal Transplant Foundation, USA
SOURCE: U.S. Pat. Appl. Publ., 9 pp., Cont.-in-part of U.S. Ser. No. 515,656.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 10
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002197242	A1	20021226	US 2002-222807	20020819
US 7019192	B2	20060328		
US 6030635	A	20000229	US 1998-31750	19980227
EP 1477176	A1	20041117	EP 2004-77080	20000222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
AT 297766	E	20050715	AT 2000-301370	20000222
ES 2241549	T3	20051101	ES 2000-301370	20000222
US 6437018	B1	20020820	US 2000-515656	20000229
CA 2457372	AA	20040219	CA 2003-2457372	20030819
WO 2004016297	A1	20040226	WO 2003-US23273	20030819
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003261248	A1	20040303	AU 2003-261248	20030819
EP 1549358	A1	20050706	EP 2003-788274	20030819
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2004197373	A1	20041007	US 2004-828316	20040421

PRIORITY APPLN. INFO.:

US 1998-31750	A2	19980227
US 1999-365880	B2	19990803
US 2000-515656	A2	20000229
EP 2000-301370	A3	20000222
US 2002-222807	A	20020819
WO 2003-US23273	W	20030819

AB The invention is directed toward a formable bone composition for application to a bone defect site to promote new bone growth at the site which comprises a new bone growth inducing compound of demineralized lyophilized allograft bone particles. The particle size ranges from about 0.1 mm to about 1.0 cm and is mixed in a hydrogel carrier containing a sodium phosphate saline buffer, the hydrogel component of the carrier ranging from about 1.0 to 5.0% of the composition and a pH between 6.8-7.4 with one or more additives of a cellular material, growth factor, demineralized bone chips or mineralized bone chips. For example, 90 g of freeze-dried demineralized cortical allograft bone were mixed into 210 g of a 4.4% solution of sodium hyaluronate in phosphate buffered saline with pH 7.3. The bone component was added to

achieve a bone concentration of 30% by weight The mixture at room temperature provided a malleable putty.

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:609852 CAPLUS
DOCUMENT NUMBER: 139:154974
TITLE: Compositions and methods for forming and strengthening bone
INVENTOR(S): Marchosky, J. Alexander
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 16 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003147860	A1	20030807	US 2002-71490	20020207
PRIORITY APPLN. INFO.:			US 2002-71490	20020207

AB Compns. are provided which stimulate bone growth. Also provided are methods for utilizing the compns. for filling in bone defects, promoting rapid fusion of bone fractures, grafts, and bone-prostheses, and promoting strengthening of osteoporotic bones. The appearance of bone formation at the site of bone defect in rat's femur was shown after application of a composition containing demineralized bone matrix, hyaluronic acid, and purified vascular endothelial growth factor at 12 wk.

L10 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:259416 CAPLUS
DOCUMENT NUMBER: 139:98598
TITLE: Chondrogenic differentiation of human mesenchymal stem cells within an alginate layer culture system
AUTHOR(S): Kavalkovich, Karl W.; Boynton, Raymond E.; Murphy, J. Mary; Barry, Frank
CORPORATE SOURCE: Osiris Therapeutics Inc., Baltimore, MD, 21231, USA
SOURCE: In Vitro Cellular & Developmental Biology: Animal (2002), 38(8), 457-466
CODEN: IVCAED; ISSN: 1071-2690
PUBLISHER: Society for In Vitro Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Human mesenchymal stem cells (hMSCs) derived from bone marrow have the capacity to differentiate along a number of connective tissue pathways and are an attractive source of chondrocyte precursor cells. When these cells are cultured in a three-dimensional format in the presence of transforming growth factor-β, they undergo characteristic morphol. changes concurrent with deposition of cartilaginous extracellular matrix (ECM). In this study, factors influencing hMSC chondrogenesis were investigated using an alginate layer culture system. Application of this system resulted in a more homogeneous and rapid synthesis of cartilaginous ECM than did micromass cultures and presented a more functional format than did alginate bead cultures. Differentiation was found to be dependent on initial cell seeding d. and was interrelated to cellular proliferation. Maximal glycosaminoglycan (GAG) synthesis defined an optimal hMSC seeding d. for chondrogenesis at 25 + 106 cells/mL. Inclusion of hyaluronan in the alginate layer at the initiation of cultures enhanced chondrogenic differentiation in a dose-dependent manger, with

maximal effect seen at 100 μg/mL. Hyaluronan increased GAG synthesis at early time points, with greater effect seen at lower cell densities, signifying cell-cell contact involvement. This culture system offers addnl. opportunities for elucidating conditions influencing chondrogenesis and for modeling cartilage homeostasis or osteoarthritic changes.

REFERENCE COUNT: 77 THERE ARE 77 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:29538 CAPLUS
DOCUMENT NUMBER: 138:78546
TITLE: Material and method for cranial bone restoration using porous calcium phosphates and bioabsorbable or biocompatible covering materials
INVENTOR(S): Inoue, Akira; Irie, Hiroyuki
PATENT ASSIGNEE(S): Olympus Optical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 6 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2003010310	A2	20030114	JP 2001-195221	20010627

PRIORITY APPLN. INFO.: JP 2001-195221 20010627

AB The materials, which restore defective parts or gaps formed between skull and resected bone piece during craniotomy, comprise (a) porous body or porous particles of Ca phosphate which show porosity 50-90%, have continuous pores having pore diameter 50-1000 μm and those having pore diameter ≤5 μm, and fill the defective parts or gaps and (b) bioabsorbable organic materials or biocompatible materials such as fibrins, poly(lactic acid), collagen, hyaluronic acid, etc., which cover the porous body or particles applied to the defects or gaps. The Ca phosphate porous body or particles may be composites with ≥1 animal growth factors selected from BMP, FGF, TGF-β, IGF, PDGF, and VEGF. The materials promote bone healing and prevent postoperative depression.

L10 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:29537 CAPLUS
DOCUMENT NUMBER: 138:78545
TITLE: Hyaluronic acid gel-based cell culture substrates for tissue regeneration
INVENTOR(S): Kato, Yukio; Tsutsumi, Shinichi; Miyazaki, Kazuko; Hara, Maiko; Kawaguchi, Hiroyuki; Kurihara, Hidemi; Miyoshi, Shozo; Hashimoto, Masamichi; Himeta, Koichi
PATENT ASSIGNEE(S): Denki Kagaku Kogyo Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 8 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2003010308	A2	20030114	JP 2001-196687	20010628

PRIORITY APPLN. INFO.: JP 2001-196687 20010628

AB The substrate is made of hyaluronic acid (I) gel which is not substantially modified with chemical crosslinking agents or chemical modifying agents and is slightly-soluble in neutral aqueous solution Animal cells, e.g.

chondrocytes, stem cells, bone marrow cells, osteoblasts, ES cells, etc., are disseminated on the substrate and the substrate containing the surviving cells is applied to defective parts of tissues to regenerate tissues, e.g. articular cartilage, costal cartilage, tracheal cartilage, skull, periodontium, cementum tendon, ligament, etc. The gel may be in the forms of sheets, films, sponges, fibers, tubes, etc., and contain bioactive substances such as cell growth factors , antibiotics, proteins, oligosaccharides, or nucleic acids. I with mol. weight 2 + 106 dalton was dissolved in H2O and the solution was adjusted to pH 1.5 with HNO3 and frozen in a flat-bottomed container at -20° for 5 days. The frozen product was soaked in a phosphate-buffered saline solution for 24 h and dried to give sponge-like gel. Rabbit femur- and tibia-derived mesenchymal cells (preparation given) were disseminated on the gel and incubated to become confluent in the presence of bFGF. Subculture was repeated twice and the 3rd subculture was implanted into a drilled hole formed in knee articular cartilage of a rabbit to promote regeneration of cartilage and bone.

L10 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:12589 CAPLUS
DOCUMENT NUMBER: 134:76442
TITLE: Compositions containing growth factors and methods for forming and strengthening bone
INVENTOR(S): Marchosky, J. Alexander
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2001000792	A1	20010104	WO 2000-US17955		20000629
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
CA 2377435	AA	20010104	CA 2000-2377435		20000629
US 6372257	B1	20020416	US 2000-606768		20000629
EP 1203074	A1	20020508	EP 2000-943309		20000629
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL					
AU 782394	B2	20050721	AU 2000-57799		20000629
PRIORITY APPLN. INFO.:			US 1999-141386P	P	19990629
			WO 2000-US17955	W	20000629

AB Compns. for stimulating bone growth comprise (a) growth factors, (b) demineralized, non-decalcified bone matrix, (c) a scaffolding material selected from cancelous bone, chitosan, chitosan-protein, and chitosan-protein fibers, and (d) a gel material selected from chitosan and its derivs., alginate, or hyaluronic acid. Addnl., compns. may contain angiogenesis-stimulating materials and osteoinductive materials. Methods for utilizing the compns. for filling in bone defects, promoting rapid fusion of bone fractures, grafts, and bone-prostheses, and promoting strengthening of osteoporotic bones are also provided. For example, bone formation at the site of bone defect was observed 12 wk after the application of the composition containing

demineralized bone matrix, hyaluronic acid, and vascular endothelial growth factor.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:911116 CAPLUS
DOCUMENT NUMBER: 134:61557
TITLE: Injectable hyaluronate-sulfated polysaccharide conjugates
INVENTOR(S): Spiro, Robert C.; Liu, Linshu
PATENT ASSIGNEE(S): Orquest, Inc., USA
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000078356	A1	20001228	WO 2000-US16793	20000616
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6288043	B1	20010911	US 1999-336005	19990618
CA 2377529	AA	20001228	CA 2000-2377529	20000616
EP 1187636	A1	20020320	EP 2000-944722	20000616
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2003502389	T2	20030121	JP 2001-504418	20000616
AU 771500	B2	20040325	AU 2000-58778	20000616

PRIORITY APPLN. INFO.: US 1999-336005 A 19990618
WO 2000-US16793 W 20000616

AB An injectable composition is provided for promoting bone and/or cartilage growth comprising hyaluronic acid cross-linked to sulfated polysaccharide through linking groups. The linking groups are diamines or amino polyalkylene glycols. The sulfated polysaccharide binds growth factors suitable for promoting tissue growth at the site of application of the composition Gels were formed by the conjugation of hyaluronic acid carrying primary amine group with heparin carrying active aldehyde group. Basic fibroblast growth factor (I) was incorporated into the gel and release kinetics of the I was studied.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:643183 CAPLUS
DOCUMENT NUMBER: 133:261923
TITLE: Inductive activity of recombinant human growth and differentiation factor-5
AUTHOR(S): Spiro, R. C.; Liu, L.-S.; Heidaran, M. A.; Thompson, A. Y.; Ng, C. K.; Pohl, J.; Poser, J. W.
CORPORATE SOURCE: Orquest, Inc., Mountain View, CA, 94043, USA
SOURCE: Biochemical Society Transactions (2000), 28(4), 362-368
CODEN: BCSTB5; ISSN: 0300-5127

PUBLISHER: Portland Press Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Growth and differentiation factor-5 (GDF-5) is a divergent member of the transforming growth factor-β/ bone morphogenetic protein (BMP) superfamily that is required for proper skeletal patterning and development in the vertebrate limb. Based on the homol. of GDF-5 with other bone-inducing BMP family members, the inductive activity of a recombinant form of human GDF-5 (rhGDF-5) was evaluated in a series of in vitro assays and in vivo bone -formation models. The in vitro response to rhGDF-5 resulted in the formation of chondrogenic nodules in fetal rat calvarial cells cultured in the context of collagen or collagen/hyaluronate extracellular matrixes. Matrixes loaded with rhGDF-5 induced ectopic cartilaginous and osseous tissue when implanted in s.c. or i.m. sites. In non-human primate long-bone-defect and spinal-fusion models, rhGDF-5 combined with a mineralized collagen matrix induced bone formation in a manner equivalent to autogenous bone. These results highlight the unique potential of rhGDF-5 in a wide variety of orthopaedic applications .
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 9 OF 12 MEDLINE on STN
ACCESSION NUMBER: 2003126541 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12605540
TITLE: Chondrogenic differentiation of human mesenchymal stem cells within an alginate layer culture system.
AUTHOR: Kavalkovich Karl W; Boynton Raymond E; Murphy J Mary; Barry Frank
CORPORATE SOURCE: Osiris Therapeutics Inc., 2000 Aliceanna Street, Baltimore, Maryland 21231, USA.
SOURCE: In vitro cellular & developmental biology. Animal, (2002 Sep) Vol. 38, No. 8, pp. 457-66.
Journal code: 9418515. ISSN: 1071-2690.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200310
ENTRY DATE: Entered STN: 19 Mar 2003
Last Updated on STN: 15 Oct 2003
Entered Medline: 14 Oct 2003
AB Human mesenchymal stem cells (hMSCs) derived from bone marrow have the capacity to differentiate along a number of connective tissue pathways and are an attractive source of chondrocyte precursor cells. When these cells are cultured in a three-dimensional format in the presence of transforming growth factor-beta, they undergo characteristic morphological changes concurrent with deposition of cartilaginous extracellular matrix (ECM). In this study, factors influencing hMSC chondrogenesis were investigated using an alginate layer culture system. Application of this system resulted in a more homogeneous and rapid synthesis of cartilaginous ECM than did micromass cultures and presented a more functional format than did alginate bead cultures. Differentiation was found to be dependent on initial cell seeding density and was interrelated to cellular proliferation. Maximal glycosaminoglycan (GAG) synthesis defined an optimal hMSC seeding density for chondrogenesis at 25 x 10(6) cells/ml. Inclusion of hyaluronan in the alginate layer at the initiation of cultures enhanced chondrogenic differentiation in a dose-dependent manner, with maximal effect seen at 100 microg/ml. Hyaluronan increased GAG synthesis at early time points, with greater effect seen at lower cell densities, signifying cell-cell contact involvement. This culture system offers additional opportunities for elucidating conditions influencing

chondrogenesis and for modeling cartilage homeostasis or osteoarthritic changes.

L10 ANSWER 10 OF 12 MEDLINE on STN
ACCESSION NUMBER: 2001114137 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10961920
TITLE: Inductive activity of recombinant human growth and differentiation factor-5.
AUTHOR: Spiro R C; Liu L; Heidaran M A; Thompson A Y; Ng C K; Pohl J; Poser J W
CORPORATE SOURCE: Orquest, Inc., 365 Ravendale Drive, Mountain View, CA 94043, USA.. bspiro@orquest.com
CONTRACT NUMBER: AR44153 (NIAMS)
SOURCE: Biochemical Society transactions, (2000) Vol. 28, No. 4, pp. 362-8.
Journal code: 7506897. ISSN: 0300-5127.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200102
ENTRY DATE: Entered STN: 22 Mar 2001
Last Updated on STN: 22 Mar 2001
Entered Medline: 15 Feb 2001

AB Growth and differentiation factor-5 (GDF-5) is a divergent member of the transforming growth factor-beta/bone morphogenetic protein (BMP) superfamily that is required for proper skeletal patterning and development in the vertebrate limb. Based on the homology of GDF-5 with other bone-inducing BMP family members, the inductive activity of a recombinant form of human GDF-5 (rhGDF-5) was evaluated in a series of in vitro assays and in vivo bone -formation models. The in vitro response to rhGDF-5 resulted in the formation of chondrogenic nodules in fetal rat calvarial cells cultured in the context of collagen or collagen/hyaluronate extracellular matrices. Matrices loaded with rhGDF-5 induced ectopic cartilaginous and osseous tissue when implanted in subcutaneous or intramuscular sites. In non-human primate long-bone-defect and spinal-fusion models, rhGDF-5 combined with a mineralized collagen matrix induced bone formation in a manner equivalent to autogenous bone. These results highlight the unique potential of rhGDF-5 in a wide variety of orthopaedic applications.

L10 ANSWER 11 OF 12 MEDLINE on STN
ACCESSION NUMBER: 1999116173 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9917648
TITLE: Potential role of fibroblast growth factor in enhancement of fracture healing.
AUTHOR: Radomsky M L; Thompson A Y; Spiro R C; Poser J W
CORPORATE SOURCE: Orquest Inc., Mountain View, CA 94043-5712, USA.
SOURCE: Clinical orthopaedics and related research, (1998 Oct) No. 355 Suppl, pp. S283-93.
Journal code: 0075674. ISSN: 0009-921X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199902
ENTRY DATE: Entered STN: 23 Feb 1999
Last Updated on STN: 3 Mar 2000
Entered Medline: 10 Feb 1999

AB Fibroblast growth factors are present in significant amounts in bone and several studies have suggested that they may be involved in normal fracture healing. It is well established that fibroblast growth factors have mitogenic and

angiogenic activity on mesoderm and neuroectoderm derived cells. Of particular interest as a member of the fibroblast growth factor family, basic fibroblast growth factor stimulates mitogenesis, chemotaxis, differentiation, and angiogenesis. It also plays an important role in the development of vascular, nervous, and skeletal systems, promotes the maintenance and survival of certain tissues, and stimulates wound healing and tissue repair. Animal studies have shown that the direct injection of fibroblast growth factor into fresh fractures stimulates callus formation, which provides mechanical stability to the fracture, accelerates healing, and restores competence. The matrix used to present the fibroblast growth factor at the fracture site plays a critical role in the effectiveness of the treatment. The evaluation of injectable basic fibroblast growth factor in a sodium hyaluronate gel for its effectiveness in stimulating fracture healing is described. When applied directly into a freshly created fracture in the rabbit fibula, a single injection of the basic fibroblast growth factor and hyaluronan results in the stimulation of callus formation, increased bone formation, and earlier restoration of mechanical strength at the fracture site. The hyaluronan gel serves as a reservoir that sequesters the basic fibroblast growth factor at the injection site for the length of time necessary to create an environment conducive to fracture healing. It is concluded that basic fibroblast growth factor and sodium hyaluronate act synergistically to accelerate fracture healing and that the combination is suitable for clinical evaluation as a therapy in fracture treatment.

L10 ANSWER 12 OF 12 MEDLINE on STN
ACCESSION NUMBER: 96212618 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8629452
TITLE: Basic fibroblast growth factor for stimulation of bone formation in osteoinductive or conductive implants.
AUTHOR: Wang J S
CORPORATE SOURCE: Department of Orthopedics, University of Lund, Sweden.
SOURCE: Acta orthopaedica Scandinavica. Supplementum, (1996 Apr) Vol. 269, pp. 1-33. Ref: 204
Journal code: 0370353. ISSN: 0300-8827.
PUB. COUNTRY: Denmark
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199606
ENTRY DATE: Entered STN: 8 Jul 1996
Last Updated on STN: 8 Jul 1996
Entered Medline: 21 Jun 1996

AB Basic Fibroblast Growth Factor (bFGF) is one of the endogenous factors found in bone matrix. bFGF is a mitogen for many cell types, including osteoblasts and chondrocytes. It can stimulate angiogenesis and osteoblast gene expression. The purpose of this study was to investigate whether exogenous bFGF can stimulate the formation of bone in bone grafts and in a bone graft substitute. In a model using demineralized bone matrix implants for bone induction, a dose of 15 ng bFGF per implant increased the number of chondrocytes and the amount of bone, whereas 1900 ng greatly inhibited cartilage and bone formation. These results are consistent with previous studies with this model, showing that a lower dose of bFGF increased bone calcium content and a higher dose reduced it. Thus, exogenous bFGF can stimulate proliferation during early phases of bone induction. A new device, the bone conduction chamber, was developed for the application of bFGF to bone conductive materials. This model made it possible to demonstrate a difference between the conductive properties of bone

grafts and porous hydroxyapatite. bFGF increased bone ingrowth into bone graft inside the chamber and showed a biphasic dose-response curve, so that 8-200 ng per implant (0.4-10 ng/mm3) increased bone ingrowth, but higher or lower doses had no effect. The same doses had the same effects in porous hydroxyapatite. In both bone grafts and porous hydroxyapatite, the highest dose still caused an increase in ingrowth of fibrous tissue. The effect on bone ingrowth was first detected after 6 weeks, regardless if administration of bFGF started at implantation or 2 weeks later, using an implanted minipump. Hyaluronate gel was effective as a slow-release carrier for bFGF. In conclusion, bFGF stimulates bone formation in bone implants, depending on dose and method for administration.

L18 ANSWER 67 OF 87 MEDLINE on STN
ACCESSION NUMBER: 2001343840 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11376106
TITLE: Synergistic roles of bone morphogenetic protein 15 and growth differentiation factor 9 in ovarian function.
AUTHOR: Yan C; Wang P; DeMayo J; DeMayo F J; Elvin J A; Carino C; Prasad S V; Skinner S S; Dunbar B S; Dube J L; Celeste A J; Matzuk M M
CORPORATE SOURCE: Department of Pathology, Baylor College of Medicine, One Baylor Plaza, Houston, TX 77030, USA.
CONTRACT NUMBER: HD-07495 (NICHD)
HD-33438 (NICHD)
SOURCE: Molecular endocrinology (Baltimore, Md.), (2001 Jun) Vol. 15, No. 6, pp. 854-66.
Journal code: 8801431. ISSN: 0888-8809.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200108
ENTRY DATE: Entered STN: 20 Aug 2001
Last Updated on STN: 20 Aug 2001
Entered Medline: 16 Aug 2001

AB Knockout mouse technology has been used over the last decade to define the essential roles of ovarian-expressed genes and uncover genetic interactions. In particular, we have used this technology to study the function of multiple members of the transforming growth factor-beta superfamily including inhibins, activins, and growth differentiation factor 9 (GDF-9 or Gdf9). Knockout mice lacking GDF-9 are infertile due to a block in folliculogenesis at the primary follicle stage. In addition, recombinant GDF-9 regulates multiple cumulus granulosa cell functions in the periovulatory period including hyaluronic acid synthesis and cumulus expansion. We have also cloned an oocyte-specific homolog of GDF-9 from mice and humans, which is termed bone morphogenetic protein 15 (BMP-15 or Bmp15). To define the function of BMP-15 in mice, we generated embryonic stem cells and knockout mice, which have a null mutation in this X-linked gene. Male chimeric and Bmp15 null mice are normal and fertile. In contrast to Bmp15 null males and Gdf9 knockout females, Bmp15 null females (Bmp15(-/-)) are subfertile and usually have minimal ovarian histopathological defects, but demonstrate decreased ovulation and fertilization rates. To further decipher possible direct or indirect genetic interactions between GDF-9 and BMP-15, we have generated double mutant mice lacking one or both alleles of these related homologs. Double homozygote females (Bmp15(-/-)Gdf9(-/-)) display oocyte loss and cysts and resemble Gdf9(-/-) mutants. In contrast, Bmp15(-/-)Gdf9(+/-) female mice have more severe fertility defects than Bmp15(-/-) females, which appear to be due to abnormalities in ovarian folliculogenesis, cumulus cell physiology, and fertilization. Thus, the dosage of intact Bmp15 and Gdf9 alleles directly influences the destiny of the oocyte during folliculogenesis and in the periovulatory period. These studies have important implications for human fertility control and the maintenance of fertility and normal ovarian physiology.

L18 ANSWER 68 OF 87 MEDLINE on STN
ACCESSION NUMBER: 2001334637 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11403716
TITLE: Differentiation stages of eosinophils characterized by hyaluronic acid binding via CD44 and responsiveness to stimuli.
AUTHOR: Watanabe Y; Hashizume M; Kataoka S; Hamaguchi E; Morimoto N; Tsuru S; Katoh S; Miyake K; Matsushima K; Tominaga M; Kurashige T; Fujimoto S; Kincade P W; Tominaga A

CORPORATE SOURCE: Department of Medical Biology, Kochi Medical School, Nankoku City, Kochi, Japan.
CONTRACT NUMBER: AI33085 (NIAID)
SOURCE: DNA and cell biology, (2001 Apr) Vol. 20, No. 4, pp. 189-202.
Journal code: 9004522. ISSN: 1044-5498.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200107
ENTRY DATE: Entered STN: 9 Jul 2001
Last Updated on STN: 9 Jul 2001
Entered Medline: 5 Jul 2001

AB To characterize interleukin (IL)-5-induced eosinophils, we examined the expression of CD44, very late antigen (VLA)-4, and the IL-5 receptor alpha chain, as well as the levels of eosinophil peroxidase and the generation of superoxide. Eosinophils were prepared from IL-5-transgenic mice, then characterized using electron microscopy to determine their responses to stimuli. Whereas CD44 densities remained almost constant, the level of VLA-4 increased in parallel with eosinophil maturation. Although a subset of IL-5-induced eosinophils with high side scatter recovered from bone marrow and rare ones found in blood recognized hyaluronic acid (HA), most did not have this property. Bone marrow eosinophils with high side scatter and lower density contained eosinophil peroxidase, not only in granules, but also in membranous structures for 30% of this population. This population developed HA-binding ability in response to IL-3, IL-4, IL-5, granulocyte-macrophage colony-stimulating factor, macrophage inflammatory protein (MIP)-2, monocyte chemotactic protein (MCP)-1, eotaxin, nerve growth factor (NGF), and opsonized zymosan (OZ). Peripheral blood eosinophils acquired HA-binding ability in response to the same stimuli, but their responses were less than those of bone marrow eosinophils with high levels of side scatter. However, splenic eosinophils did not respond to these stimuli. Although peripheral blood eosinophils did not proliferate when stimulated by IL-5, these were the only cells that released eosinophil peroxidase in response to IL-4, MIP-2, MCP-1, eotaxin, NGF, and OZ. With the exception of a subset of bone marrow eosinophils, the ability to acquire HA binding, but not the ability to generate superoxide, correlated with eosinophil peroxidase activity and major basic protein accumulation in the granules of maturing cells.

L18 ANSWER 69 OF 87 MEDLINE on STN
ACCESSION NUMBER: 2001116865 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11155688
TITLE: Morphological study on cell-cell interaction between osteoclasts and osteoblasts.
AUTHOR: Nakamura H
CORPORATE SOURCE: First Department of Oral Anatomy, Okayama University School of Dentistry, 2-5-1 Shikata-cho, Okayama 700-8525 Japan.
SOURCE: Kaibogaku zasshi. Journal of anatomy, (2000 Oct) Vol. 75, No. 5, pp. 427-32. Ref: 31
Journal code: 0413526. ISSN: 0022-7722.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200102
ENTRY DATE: Entered STN: 22 Mar 2001
Last Updated on STN: 22 Mar 2001
Entered Medline: 15 Feb 2001

AB We reviewed morphological characteristics in cell-cell interaction between

osteoclasts and the cells of osteoblast lineage. Heparan sulfate proteoglycans (HSPG) are localized in the intercellular space between osteoblasts and osteoclasts. HSPG is involved in reservation of heparin binding growth factors (HBGF), protection from proteolysis of HBGF, and ligand-receptor interaction in the case of fibroblast growth factors. HSPG may play an important role in cell-cell interaction between osteoblasts and osteoclasts by reserving HBGF and heparin binding adhesion molecules such as fibronectin. On the other hand, CD44, a hyaluronate receptor, and moesin are colocalized in the basolateral plasma membrane of osteoclasts. Calcitonin changes their localization in osteoclasts, suggesting that the CD44-moesin-actin filament system is engaged in the regulation of cell polarity. Although hyaluronates colocalize with CD44 in the basolateral membrane of osteoclasts, the precise intracellular signaling mechanism needs to be clarified in further research. Bone metabolism may be regulated by cell-cell and cell-matrix interaction among bone cells via adhesion molecule, extracellular matrices and cytokines.

L18 ANSWER 70 OF 87 MEDLINE on STN
ACCESSION NUMBER: 2000268126 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10806045
TITLE: An analysis of 14 molecular markers for monitoring osteoarthritis: segregation of the markers into clusters and distinguishing osteoarthritis at baseline.
AUTHOR: Otterness I G; Swindell A C; Zimmerer R O; Poole A R; Ionescu M; Weiner E
CORPORATE SOURCE: Inflammation Biology, Pfizer Central Research, Groton, CT 06340, USA.. otterx@earthlink.net
SOURCE: Osteoarthritis and cartilage / OARS, Osteoarthritis Research Society, (2000 May) Vol. 8, No. 3, pp. 180-5. Journal code: 9305697. ISSN: 1063-4584.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200008
ENTRY DATE: Entered STN: 11 Aug 2000
Last Updated on STN: 11 Aug 2000
Entered Medline: 3 Aug 2000

AB OBJECTIVE: To investigate the relationships between serum and urinary molecular markers (MM) used to monitor osteoarthritis. DESIGN: Forty osteoarthritis patients had blood and urine collected at baseline and 1, 3, 6 and 12 months later. Specimens from 20 controls were obtained twice at a one month interval. The concentration of 14 different markers was determined at each time point and the data were analyzed by statistical methodology. RESULTS: The markers could be divided by the method of principal components analysis into five clusters of related markers: inflammation markers (C-reactive protein, tumor necrosis receptor type I and tumor necrosis receptor type II, interleukin 6, eosinophilic cationic protein), bone markers (bone sialoprotein, hydroxylysyl pyridinoline, lysyl pyridinoline), putative markers of cartilage anabolism (carboxypropeptide of type II procollagen, hyaluronan, epitope 846) and catabolism (keratan sulfate, cartilage oligomeric matrix protein), and transforming growth factor beta. Three markers (tumor necrosis factor receptor II, cartilage oligomeric matrix protein and epitope 846) from independent clusters discriminated osteoarthritis patients from controls. Inflammation was not a confounding factor in measurement, but a recognizable distinguishing factor in osteoarthritis. CONCLUSIONS: The markers separated into rational groups on the basis of their covariance, a finding with independent biochemical support. The covariance of markers from the same cluster suggests the use of a representative marker from the cluster to reflect changes in osteoarthritis. If multiple markers are

being measured within a single cluster, then the use of a weighted cluster 'factor' may be preferable to the separate use of individual markers.

L18 ANSWER 71 OF 87 MEDLINE on STN
ACCESSION NUMBER: 2000079418 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10611546
TITLE: Engineering of osteochondral tissue with bone marrow mesenchymal progenitor cells in a derivatized hyaluronan-gelatin composite sponge.
AUTHOR: Angele P; Kujat R; Nerlich M; Yoo J; Goldberg V; Johnstone B
CORPORATE SOURCE: Department of Orthopaedics, Case Western Reserve University, Cleveland, OH 44106-5000, USA.
CONTRACT NUMBER: AR-37726 (NIAMS)
AR-44390 (NIAMS)
SOURCE: Tissue engineering, (1999 Dec) Vol. 5, No. 6, pp. 545-54.
Journal code: 9505538. ISSN: 1076-3279.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200005
ENTRY DATE: Entered STN: 25 May 2000
Last Updated on STN: 25 May 2000
Entered Medline: 15 May 2000

AB The aim of this study was to investigate the potential of a composite matrix, containing esterified hyaluronic acid and gelatin, to facilitate the osteochondral differentiation of culture-expanded, bone marrow-derived mesenchymal progenitor cells. The cell loading characteristics and the effects of the matrix on cell differentiation were examined in vitro and in vivo. Empty and cell-loaded composites were cultivated for up to 28 days in a chemically defined medium with or without transforming growth factor -beta1 (TGF-beta1). A type II collagen-rich extracellular matrix was produced by cells loaded in the matrix and cultured in the presence of TGF-beta1. Empty and cell-loaded matrices were also implanted subcutaneously in immunodeficient mice. Three types of implant were used: empty (group I), cell-loaded matrices (Group II), and cell-loaded matrices cultured for 14 days in vitro in defined medium with TGF-beta1 (group III). No osteochondral differentiation was found in implanted empty matrices; however, the matrix supported osteochondrogenic cell differentiation in the cell-loaded implants. Preculture in vitro in a chondrogenic medium increased the percentage of osteochondral tissue found in the constructs after 3 weeks. These results indicate the potential use of this composite matrix for delivery of bone marrow-derived mesenchymal progenitor cells for the repair of chondral and osseous defects. The results also indicate that this composite matrix is useful for in vitro tissue engineering.

L18 ANSWER 72 OF 87 MEDLINE on STN
ACCESSION NUMBER: 1999329059 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10400671
TITLE: Fibulin-1 is a ligand for the C-type lectin domains of aggrecan and versican.
AUTHOR: Aspberg A; Adam S; Kostka G; Timpl R; Heinegard D
CORPORATE SOURCE: Department of Cell and Molecular Biology, Section for Connective Tissue Biology, Lund University, P. O. Box 94, SE-221 00 Lund, Sweden.. anders.aspberg@medlem.lu.se
SOURCE: The Journal of biological chemistry, (1999 Jul 16) Vol. 274, No. 29, pp. 20444-9.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English

FILE SEGMENT: Priority Journals
ENTRY MONTH: 199908
ENTRY DATE: Entered STN: 27 Aug 1999
Last Updated on STN: 3 Mar 2000
Entered Medline: 19 Aug 1999

AB The aggregating proteoglycans (aggrecan, versican, neurocan, and brevican) are important components of many extracellular matrices. Their N-terminal globular domain binds to hyaluronan, but the function of their C-terminal region containing a C-type lectin domain is less clear. We now report that a 90-kDa protein copurifies with recombinant lectin domains from aggrecan and versican, but not from the brain-specific neurocan and brevican. Amino acid sequencing of tryptic peptides from this protein identified it as fibulin-1. This extracellular matrix glycoprotein is strongly expressed in tissues where versican is expressed (blood vessels, skin, and developing heart), and also expressed in developing cartilage and bone. It is thus likely to interact with these proteoglycans in vivo. Surface plasmon resonance measurements confirmed that aggrecan and versican lectin domains bind fibulin-1, whereas brevican and neurocan do not. As expected for a C-type lectin, the interactions with fibulin-1 are Ca2+-dependent, with KD values in the low nanomolar range. Using various deletion mutants, the binding site for aggrecan and versican lectin domains was mapped to the epidermal growth factor-like repeats in domain II of fibulin-1. No difference in affinity was found for deglycosylated fibulin-1, indicating that the proteoglycan C-type lectin domains bind to the protein part of fibulin-1.

L18 ANSWER 73 OF 87 MEDLINE on STN
ACCESSION NUMBER: 97351373 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9207655
TITLE: Regional differences of dura osteoinduction: squamous dura induces osteogenesis, sutural dura induces chondrogenesis and osteogenesis.
AUTHOR: Yu J C; McClintock J S; Gannon F; Gao X X; Mobasser J P; Sharawy M
CORPORATE SOURCE: Division of Plastic Surgery, Medical College of Georgia, Augusta 30912-4080, USA.
SOURCE: Plastic and reconstructive surgery, (1997 Jul) Vol. 100, No. 1, pp. 23-31.
Journal code: 1306050. ISSN: 0032-1052.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199707
ENTRY DATE: Entered STN: 5 Aug 1997
Last Updated on STN: 5 Aug 1997
Entered Medline: 24 Jul 1997

AB Dura plays an important role in calvarial morphogenesis. However, precisely what that role is remains unclear. We present here in vivo evidence that dura without other central nervous system components induces both chondrogenesis and osteogenesis. The mechanism is, at least in part, by proximate tissue interaction. The objectives of this experiment were to answer the following: (1) Can dura actually induce osteogenesis without the influence of the underlying brain? (2) What are the requirements of this dura-induced heterotopic osteogenesis? (3) What are the differences between dura underlying sutures and dura underlying the squamous portions of the cranial bones? Dura underlying the metopic, sagittal, and lambdoidal sutures and dura underlying the flat portions of frontal and parietal bones were obtained from neonatal Lewis rats and transplanted into the posterior thoraces of adult Lewis recipients. In group I, dura underlying the metopic, sagittal, and lambdoidal sutures (n = 20) and dura underlying the flat portions of frontal and parietal bones (n = 20) were transplanted individually into separate epitheliomesenchymal pockets. Group II animals had dura underlying the

metopic, sagittal, and lambdoidal sutures (n = 10) and dura underlying the flat portions of frontal and parietal bones (n = 10) transplanted individually into surgically created mesenchymal pockets by placing the dura grafts between panniculus carnosus and latissimus dorsi muscles. The animals were sacrificed at 2-week intervals. Light microscopy, special histochemical analysis, immunohistochemistry, and electron microscopy were performed. Bone formation was seen in 15 of the 18 animals (83 percent) in group I. No bone or cartilage formation was seen in group II. Chondrogenesis was seen in 4 animals receiving dura underlying the metopic, sagittal, and lambdoidal sutures in group I. Cellular hyperproliferation was seen at 2 weeks when dura was transplanted close to the hair follicles. These cells had a high nucleus-to-cytoplasm ratio and were positive for transforming growth factor beta. This hyperproliferation was followed by production and accumulation of Alcian blue-positive extracellular matrix that resisted digestion by hyaluronidase. Cellularly active cartilage was seen at 6 weeks. There was no chondrogenesis in animals receiving dura underlying the flat portions of frontal and parietal bones in group I. Electron microscopy demonstrated the presence of proteoglycan-like ground substance and type II collagen in the inner layer of sutural dura and the predominance of dense type I collagen in the squamous dura and the external layer of the sutural dura. The important findings of this experiment are that (1) heterotopically transplanted neonatal dura can induce osteogenesis, (2) this heterotopic osteoinduction by dura requires epitheliomesenchymal interaction, and (3) separating dura into sutural dura and squamous dura, chondrogenesis occasionally occurred in addition to osteogenesis with the former, while only membranous ossification occurred with the latter, indicating intrinsic differences within the dura mater. This dural heterogeneity is supported by direct ultrastructural data.

L18 ANSWER 74 OF 87 MEDLINE on STN
ACCESSION NUMBER: 97307858 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9182706
TITLE: Nitric oxide degradation of heparin and heparan sulphate.
AUTHOR: Vilar R E; Ghael D; Li M; Bhagat D D; Arrigo L M; Cowman M K; Dweck H S; Rosenfeld L
CORPORATE SOURCE: Neonatal Research Laboratory, Division of Neonatology-Perinatology, Department of Pediatrics, New York Medical College, Valhalla, NY 10595, USA.
SOURCE: The Biochemical journal, (1997 Jun 1) Vol. 324 (Pt 2), pp. 473-9.
Journal code: 2984726R. ISSN: 0264-6021.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199707
ENTRY DATE: Entered STN: 21 Jul 1997
Last Updated on STN: 21 Jul 1997
Entered Medline: 8 Jul 1997

AB NO is a bioactive free radical produced by NO synthase in various tissues including vascular endothelium. One of the degradation products of NO is HNO2, an agent known to degrade heparin and heparan sulphate. This report documents degradation of heparin by cultured endothelial-cell-derived as well as exogenous NO. An exogenous narrow molecular-mass preparation of heparin was recovered from the medium of cultured endothelial cells using strong-anion exchange. In addition, another narrow molecular-mass preparation of heparin was gassed with exogenous NO under argon. Degradation was evaluated by gel-filtration chromatography. Since HNO2 degrades heparin under acidic conditions, the reaction with NO gas was studied under various pH conditions. The results show that the degradation of exogenous heparin by endothelial cells is inhibited by NO synthase inhibitors. Exogenous NO gas at concentrations as low as 400

p.p.m. degrades heparin and heparan sulphate. Exogenous NO degrades heparin at neutral as well as acidic pH. Endothelial-cell-derived NO, as well as exogenous NO gas, did not degrade hyaluronan, an unrelated glycosaminoglycan that resists HNO2 degradation. Peroxynitrite, a metabolic product of the reaction of NO with superoxide, is an agent that degrades hyaluronan; however, peroxynitrite did not degrade heparin. Thus endothelial-cell-derived NO is capable of degrading heparin and heparan sulphate via HNO2 rather than peroxynitrite. These observations may be relevant to various pathophysiological processes in which extracellular matrix is degraded, such as bone development, apoptosis, tissue damage from inflammatory responses and possible release of growth factors and cytokines.

L18 ANSWER 75 OF 87 MEDLINE on STN
ACCESSION NUMBER: 97136503 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8981904
TITLE: Basic fibroblast growth factor promotes bone ingrowth in porous hydroxyapatite.
AUTHOR: Wang J S; Aspenberg P
CORPORATE SOURCE: Department of Orthopedics, Lund University Hospital, Sweden.
SOURCE: Clinical orthopaedics and related research, (1996 Dec) No. 333, pp. 252-60.
Journal code: 0075674. ISSN: 0009-921X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199701
ENTRY DATE: Entered STN: 19 Feb 1997
Last Updated on STN: 6 Feb 1998
Entered Medline: 30 Jan 1997

AB The effect of basic fibroblast growth factor on tissue ingrowth and differentiation in porous hydroxyapatite of coralline origin was studied in a bone chamber model. The hydroxyapatite with or without basic fibroblast growth factor was placed in 22 mm3 titanium bone conduction chambers implanted bilaterally in rat tibiae. Ingrowing bone could enter the cylindrical interior of the chamber only at 1 end. It then penetrated the porous hydroxyapatite inside the chamber. The distance that the ingrown tissue had reached into the material then was measured on histologic slides. Because fibrous tissue always reached further into the material than did bone, both total tissue ingrowth and bone ingrowth distances were measured. In implants supplemented with 0.04 microg basic fibroblast growth factor in a hyaluronate gel carrier, the bone ingrowth distance was increased by 70% at 6 weeks, as compared with paired controls in the contralateral leg. The total tissue ingrowth distance also was increased by 58%. When the dose of basic fibroblast growth factor was increased to 1.0 microg, still using the hyaluronate carrier, there was no difference in bone ingrowth compared with controls, but this dose still increased the total tissue ingrowth. In hydroxyapatite with 1.5 microg basic fibroblast growth factor without hyaluronate gel at 4 weeks, no increase in bone ingrowth was shown, but total tissue ingrowth was increased. At 6 weeks, bone ingrowth and total tissue ingrowth were increased by 41% and 33%, respectively. With a lower dose of 0.15 microg without carrier, only the total ingrowth distance was increased. The results suggest that basic fibroblast growth factor may promote tissue ingrowth into porous hydroxyapatite and that bone ingrowth may be increased by appropriate doses. The hyaluronate gel carrier reduced the optimal dose.

L18 ANSWER 76 OF 87 MEDLINE on STN

ACCESSION NUMBER: 97123729 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8954864
TITLE: BMEC-1: a human bone marrow microvascular endothelial cell line with primary cell characteristics.
AUTHOR: Candal F J; Rafii S; Parker J T; Ades E W; Ferris B; Nachman R L; Kellar K L
CORPORATE SOURCE: Biological Products Branch, Scientific Resources Program, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia 30333, USA.
CONTRACT NUMBER: K08-HL02926 (NHLBI)
SOURCE: Microvascular research, (1996 Nov) Vol. 52, No. 3, pp. 221-34.
Journal code: 0165035. ISSN: 0026-2862.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199703
ENTRY DATE: Entered STN: 27 Mar 1997
Last Updated on STN: 27 Mar 1997
Entered Medline: 19 Mar 1997

AB Bone marrow microvascular endothelial cells (BMEC) are a functional component of the bone marrow stroma and have been shown to release hematopoietic regulatory factors as well as to selectively adhere and support the proliferation and differentiation of CD34+ hematopoietic progenitors. An early passage of these cells was immortalized by transfection with a vector (pSVT) encoding the large T antigen of SV40. The transformed cell line (CDC/CU.BMEC-1) expresses the SV40 transcript, retains the primary cell expression of Ulex europeaus and vWF/ FVIII, and incorporates acetylated low-density lipoprotein. In addition, BMEC-1 mirrors the phenotype of the primary cells with only a few exceptions. Both cell populations express the cellular adhesion molecules ICAM-1 and PECAM and also VCAM-1 and ELAM-1 after upregulation by tumor necrosis factor-alpha. The fibronectin receptor, hyaluronate receptor, collagen receptor, integrins VLA-alpha 3, VLA-alpha 4, and beta 4, endoglin, collagen IV, CD58, and CD61 are also expressed. The only differences are that BMEC-1 expresses higher levels of ICAM-1, CD58, CD34, CD36, and c-kit than the primary cells. The supernatants of primary cell and BMEC-1 contain stem cell factor, interleukin-6 (IL-6), granulocyte-macrophage colony-stimulating factor (GM-CSF), IL-1 alpha, IL-11, and G-CSF. The functional significance of these hematopoietic cytokines was demonstrated in transwell cultures. Both cell populations supported the expansion of progeny from CD34+ cell-enriched cord blood mononuclear cells suspended in the upper chamber. These characteristics, plus the fact that BMEC-1 can be maintained independently of exogenous growth factors and exhibit contact inhibition, indicate that this cell line can be used to further define the role of BMEC in hematopoiesis.

L18 ANSWER 77 OF 87 MEDLINE on STN
ACCESSION NUMBER: 96383417 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8791281
TITLE: Exogenous glycosaminoglycans (GAG) differentially modulate GAG synthesis by anchorage-independent cultures of the outer cells from neonatal rat calvaria in the absence and presence of TGF-beta.
AUTHOR: Anastassiades T P; Chopra R K; Wood A
CORPORATE SOURCE: Department of Medicine, Queen's University, Kingston, Ontario, Canada.
SOURCE: Molecular and cellular biochemistry, (1996 May 10) Vol. 158, No. 1, pp. 25-32.
Journal code: 0364456. ISSN: 0300-8177.
PUB. COUNTRY: Netherlands

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199703
ENTRY DATE: Entered STN: 27 Mar 1997
Last Updated on STN: 27 Mar 1997
Entered Medline: 17 Mar 1997

AB In anchorage-dependent (AD) cultures of the outer cell population (OCP) from neonatal rat calvaria, transforming growth factor -beta 1 (TGF-beta) specifically upregulated the synthesis of chondroitin sulfate (CS) proteoglycan (PG) and uncoupled the inhibitory effect of increasing cell density on CS PG synthesis (reference #30). Utilizing the same cell population, we have further examined the possibility that glycosaminoglycans (GAG) known to be synthesized and secreted by bone cells might exert feedback effects on GAG synthesis and/or its stimulation by TGF-beta. Although addition of TGF-beta alone stimulated net synthesis of HA and CS in both AD and anchorage-independent (AI) cultures, significant alterations of basal and TGF-beta-stimulated GAG synthesis by exogenous GAGs were observed only in AI cultures. In AI cultures exogenously added hyaluronic acid (HA) markedly enhanced the basal synthesis of HA and CS while heparin (H) suppressed the basal synthesis of HA, CS as well as dermatan sulfate (DS). Also, the addition of HA markedly potentiated the stimulation by TGF-beta of HA and CS synthesis as did heparan sulfate (HS) for CS and DS synthesis. H suppressed the stimulation of the synthesis of HA, CS and DS by TGF-beta. Overall, our results indicate specific effects of individual GAGs on basal and TGF-beta-stimulated GAG synthesis in OCP cultures. We suggest that some of the GAGs in the OCP microenvironment (which with the exception of HA are covalently linked to protein cores of secreted PGs), acting in concert with TGF-beta, may serve as an amplification system for upregulating GAG synthesis in the rapidly growing neonatal calvarium.

L18 ANSWER 78 OF 87 MEDLINE on STN
ACCESSION NUMBER: 95081311 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7989496
TITLE: Comment: effect of cytokines on prolactin production by human decidual stromal cells in culture: studies using cells freed of bone marrow-derived contaminants.
AUTHOR: Vicovac L M; Starkey P M; Aplin J D
CORPORATE SOURCE: INEP, University of Belgrade, Zemun, Yugoslavia.
SOURCE: The Journal of clinical endocrinology and metabolism, (1994 Dec) Vol. 79, No. 6, pp. 1877-82.
Journal code: 0375362. ISSN: 0021-972X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199501
ENTRY DATE: Entered STN: 24 Jan 1995
Last Updated on STN: 24 Jan 1995
Entered Medline: 12 Jan 1995

AB Human decidua contains resident decidual cells alongside a population of bone marrow-derived cells, among which macrophages and large granular lymphocytes are most abundant. We hypothesized that soluble effectors produced by bone marrow-derived cells may modulate the function of the decidual cells. To investigate this, a cell purification protocol was devised that involved digestion of first-trimester decidua with collagenase and hyaluronidase to produce a mixed stromal cell suspension from which the bone marrow-derived cells were removed using immunomagnetic beads coated with anti-CD45. The resulting stromal cells were maintained in culture in the presence of progesterone and were found to produce PRL. The effect of a panel of cytokines on PRL production was examined. Tumor necrosis factors-alpha and -beta had a dose-dependent inhibitory effect, and tumor necrosis factor receptors were

identified on the cells. Interleukin 1 alpha and 1 beta, platelet-derived growth factor, and transforming growth factor-beta 1 were also found to inhibit PRL production, and platelet-derived growth factor and transforming growth factor-beta 1 stimulated cell proliferation. These findings suggest an interaction between the immune and endocrine systems in regulating the maternal environment of early pregnancy.

L18 ANSWER 79 OF 87 MEDLINE on STN
ACCESSION NUMBER: 94358448 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7521370
TITLE: Monocyte adhesion in patients with bone marrow fibrosis is required for the production of fibrogenic cytokines. Potential role for interleukin-1 and TGF-beta.
AUTHOR: Rameshwar P; Denny T N; Stein D; Gascon P
CORPORATE SOURCE: Department of Medicine, UMDNJ-New Jersey Medical School, Newark 07103.
SOURCE: Journal of immunology (Baltimore, Md. : 1950), (1994 Sep 15) Vol. 153, No. 6, pp. 2819-30.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199410
ENTRY DATE: Entered STN: 13 Oct 1994
Last Updated on STN: 29 Jan 1996
Entered Medline: 5 Oct 1994

AB Idiopathic myelofibrosis (IMF) is a hemologic disorder characterized by bone marrow (BM) fibrosis. The BM contains excessive deposits of extracellular matrix proteins and exhibits neovascularization. The fibrosis is hypothesized to be a reactive phenomenon secondary to a clonal myeloid disorder. Growth factors such as platelet-derived growth factor (PDGF), TGF-beta, and epidermal growth factor have been postulated as potential agents involved in BM fibrosis. We studied the induction of two fibrogenic cytokines, IL-1 and TGF-beta, in IMF monocytes. High levels of both cytokines were produced in unstimulated IMF monocytes, compared with background levels produced in normal controls. Most of the TGF-beta produced by IMF monocytes was in its active form. The spontaneous induction of IL-1 alpha, IL-1 beta, and TGF-beta in IMF monocytes parallels an increase in their steady state mRNA. Although high levels of cytoplasmic IL-1 alpha, IL-1 beta, and TGF-beta protein were detected in monocytes that were not subjected to any form of adherence, the secretion of these cytokines required adhesion. High levels of fibronectin, hyaluronic acid, and collagen, all potential ligands for the CD44 adhesion molecule, have been reported in the circulation of IMF patients. However, the Ab-binding capacity of CD44 in IMF monocytes was reduced by 50% when compared with normal controls. Our results indicate that monocytes and adhesion molecules may play a role in the induction of fibrogenic cytokines. These parameters may be important to the pathophysiology of BM fibrosis.

L18 ANSWER 80 OF 87 MEDLINE on STN
ACCESSION NUMBER: 94285157 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8014937
TITLE: Differential effects of bone associated factors on newly synthesized anionic glycoconjugates by articular chondrocyte cultures from adult and immature bovines.
AUTHOR: Howard S; Anastassiades T
CORPORATE SOURCE: Department of Medicine, Queen's University, Kingston, ON, Canada.
SOURCE: The Journal of rheumatology, (1993 Dec) Vol. 20, No. 12, pp. 2083-94.

Journal code: 7501984. ISSN: 0315-162X.
PUB. COUNTRY: Canada
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199407
ENTRY DATE: Entered STN: 10 Aug 1994
Last Updated on STN: 10 Aug 1994
Entered Medline: 26 Jul 1994

AB OBJECTIVE. To determine if bone associated peptide factors (BAF) differentially affect proteoglycan and hyaluronic acid (HA) synthesis as a result of the maturity of the animal and of the location of chondrocytes within cartilage zones. METHODS. Calf and adult bovine articular chondrocytes were isolated and cultured, as high density monolayers, with 3H-glucosamine and 35S-sulfate. The effects of commercial transforming growth factor beta (TGF-beta) and a preparation from bovine bone that contained the total extractable stimulatory activity for glycosaminoglycan (GAG) synthesis (matrigenin activity) were studied. RESULTS. Calf chondrocytes spontaneously synthesized a higher proportion of proteoglycans of larger hydrodynamic size, but the addition of the BAF resulted in a proportionally greater shift in the adult chondrocytes towards the synthesis of larger proteoglycans, appearing in the medium. Subpopulations of adult chondrocytes from the deep zone synthesized spontaneously more chondroitin sulfate (CS) and less HA than chondrocytes from the superficial zone, but the calf chondrocytes from the 3 zones showed similar patterns of GAG synthesis. Adult chondrocytes from the deep zone had large responses to the BAF for HA but not CS synthesis, resembling the subpopulations of the calf chondrocytes. CONCLUSION. BAF differentially modulate HA and CS synthesis of articular chondrocytes as a result of maturation and topography. We speculate as to how this differential response to BAF may help set the stage for the progression of osteoarthritis in weight bearing joints.

L18 ANSWER 81 OF 87 MEDLINE on STN
ACCESSION NUMBER: 94033524 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7693037
TITLE: Human acute myeloid leukemia cells bind to bone marrow stroma via a combination of beta-1 and beta-2 integrin mechanisms.
AUTHOR: Bendall L J; Kortlepel K; Gottlieb D J
CORPORATE SOURCE: Department of Haematology, Westmead Hospital, Westmead New South Wales, Sydney, Australia.
SOURCE: Blood, (1993 Nov 15) Vol. 82, No. 10, pp. 3125-32.
Journal code: 7603509. ISSN: 0006-4971.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199312
ENTRY DATE: Entered STN: 17 Jan 1994
Last Updated on STN: 29 Jan 1996
Entered Medline: 22 Dec 1993

AB Acute myeloid leukemia (AML) cells respond to exogenous stimulation from myeloid growth factors that may be secreted by cells of the bone marrow (BM) stroma and retained by glycosaminoglycans in the extracellular matrix. We have analyzed the capacity of malignant cells from patients with AML to maintain close proximity to sites of growth factor production and retention by binding to BM stromal elements, including fibroblasts and extracellular matrix proteins. Leukemic cells from all cases of AML adhered to BM fibroblast (BMF) monolayers (mean +/- standard error [SE] percentage binding, 30.9% +/- 2.5%; n = 23) and to fibronectin and laminin (mean +/- SE percentage binding, 28.0% +/- 4.1% [n = 11] and 21.5% +/-

2.3% [n = 8], respectively). Binding to bovine and human collagen type 1, vitronectin, hyaluronic acid, and albumin was minimal. Analysis of binding mechanisms indicated that very late antigen-4 (VLA-4) and VLA-5 were responsible for AML cell binding to fibronectin. Binding to laminin could be inhibited by antibody to the alpha chain of VLA-6. In contrast, AML cell adhesion to BMF monolayers was not impaired by blocking antibodies to either beta 1 or beta 2 integrins used alone, although the combination of anti-CD11/CD18 and anti-VLA-4 inhibited binding in more than 50% of cases. When anti-VLA-5 was added in these cases, mean +/- SE inhibition of binding of 45.5% +/- 9.1% (P < .001) was observed. Binding of AML cells to extracellular matrix proteins fibronectin and laminin is predominantly beta 1-integrin-dependent, but AML cell adhesion to BMF relies on the simultaneous involvement of beta 1 and beta 2 integrins as well as other currently unrecognized ligands.

L18 ANSWER 82 OF 87 MEDLINE on STN
ACCESSION NUMBER: 93353878 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8350618
TITLE: Human acute myeloid leukaemia cells express adhesion proteins and bind to bone marrow fibroblast monolayers and extracellular matrix proteins.
AUTHOR: Kortlepel K; Bendall L J; Gottlieb D J
CORPORATE SOURCE: Department of Haematology, Westmead Hospital, NSW, Australia.
SOURCE: Leukemia : official journal of the Leukemia Society of America, Leukemia Research Fund, U.K, (1993 Aug) Vol. 7, No. 8, pp. 1174-9.
Journal code: 8704895. ISSN: 0887-6924.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199309
ENTRY DATE: Entered STN: 1 Oct 1993
Last Updated on STN: 3 Feb 1997
Entered Medline: 10 Sep 1993

AB Adhesion protein expression by acute myeloid leukaemia (AML) cells may affect bone marrow stromal localization and determine exposure of leukaemic cells to stromal derived myeloid growth factors. We have analysed the surface expression by myeloid leukaemic cells of proteins with known adhesive function and the ability of AML cells to adhere to bone marrow fibroblasts and the extracellular matrix proteins fibronectin and laminin. Cells from all six patients tested adhered to bone marrow fibroblast monolayers (mean binding 28.8 +/- 12.8%) and to purified fibronectin in five cases studied (mean binding 33.8 +/- 15.3%). Cells from four patients with AML also adhered to laminin (mean binding 20.9 +/- 4.0%). AML cells from the majority of patients with leukaemia at diagnosis or relapse expressed the ligand pair LFA-1 and ICAM-1, the CD2 ligand LFA-3, alpha and beta chains of the integrins VLA-4, VLA-5 and VLA-6, and the hyaluronate receptor CD44. Antibodies to CD11a, CD18, VLA-4 alpha, and VLA-5 alpha failed to inhibit binding of AML cells to bone marrow fibroblasts but anti-VLA-5 alpha antibodies inhibited AML cell binding to fibronectin by approximately 50%. The ability of AML cells to adhere to bone marrow fibroblasts and extracellular matrix proteins such as fibronectin and laminin may to help explain the capacity of AML cells to persist in the marrow during periods of apparent complete remission and to subsequently proliferate under the influence of locally secreted myeloid growth factors.

L18 ANSWER 83 OF 87 MEDLINE on STN
ACCESSION NUMBER: 93293967 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8514850
TITLE: Hyaluronate activation of CD44 induces insulin-like growth

factor-1 expression by a tumor necrosis factor-alpha-dependent mechanism in murine macrophages.
AUTHOR: Noble P W; Lake F R; Henson P M; Riches D W
CORPORATE SOURCE: Department of Pediatrics, National Jewish Center for Immunology and Respiratory Medicine, Denver, Colorado 80206.
CONTRACT NUMBER: HL-27353 (NHLBI)
SOURCE: The Journal of clinical investigation, (1993 Jun) Vol. 91, No. 6, pp. 2368-77.
Journal code: 7802877. ISSN: 0021-9738.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199307
ENTRY DATE: Entered STN: 6 Aug 1993
Last Updated on STN: 6 Aug 1993
Entered Medline: 21 Jul 1993

AB Macrophages participate in inflammatory and repair processes in part through the selective release of cytokines that contribute to tissue remodeling. Extracellular matrix components generated at inflammatory sites may influence tissue remodeling by effects on leukocyte adherence and local cytokine production. In murine bone marrow-derived macrophages, we found that soluble hyaluronic acid stimulated IL-1 beta, TNF alpha, and insulin-like growth factor-1 (IGF-1) mRNA transcript expression as well as IGF-1 protein synthesis. Monoclonal antibodies to the hyaluronic acid receptor CD44 blocked the effects of hyaluronic acid on IL-1 beta, TNF alpha, and IGF-1 expression. TNF alpha and IL-1 beta mRNA expression preceded IGF-1 protein synthesis, and TNF alpha, but not IL-1 beta, was found to directly stimulate IGF-1. Furthermore, IGF-1 induction was dependent on endogenous TNF alpha production since IGF-1 protein synthesis was inhibited in the presence of anti-TNF alpha antiserum. In addition, IL-1 beta was found to exert a regulatory role on IGF-1 production by enhancing the TNF alpha effect. IL-1 beta and TNF alpha mRNA transcript expression as well as IGF-1 protein synthesis were also stimulated by chrysotile asbestos. Anti-CD44 antibodies had no effect whereas anti-TNF alpha antiserum blocked asbestos-stimulated IGF-1 production. These results indicate that hyaluronate activation of CD44 induces cytokine expression and macrophage-derived IGF-1 production is dependent on TNF alpha expression.

L18 ANSWER 84 OF 87 MEDLINE on STN
ACCESSION NUMBER: 91215470 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2090332
TITLE: Newly synthesized proteoglycans secreted by sequentially derived populations of cells from new-born rat calvaria: effects of transforming growth factor-beta and matrigenin activity.
AUTHOR: Chopra R K; Li Z M; Vickery S; Anastassiades T
CORPORATE SOURCE: Department of Medicine, Queen's University, Kingston, Ontario, Canada.
SOURCE: Cell differentiation and development : the official journal of the International Society of Developmental Biologists, (1990 Oct) Vol. 32, No. 1, pp. 47-59.
Journal code: 8811335. ISSN: 0922-3371.
PUB. COUNTRY: Ireland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199106
ENTRY DATE: Entered STN: 23 Jun 1991
Last Updated on STN: 3 Feb 1997
Entered Medline: 3 Jun 1991

AB Three populations (1, 3 and 6) of bone cells, derived from rat calvaria by sequential enzymatic digestion, were cultured with [3H]glucosamine and [35S]sulfate, in the presence or absence of transforming growth factor-beta (TGF-beta) or bone-derived matrigenin activity. Population 6 synthesized a chondroitin sulfate proteoglycan (PG) and responded to the addition of the factors by increased rates of synthesis of hyaluronic acid (HA) and PG and an increase in the size of the HA. Comparisons of populations 1, 3 and 6 showed an ordered, spontaneous increase in HA and PG synthesis. However, the addition of matrigenin activity resulted in a much greater stimulation of PG, but not HA, synthesis in population 1 compared to population 6, suggesting a cellular organization in the calvarium whose net effect would be to direct PG synthesis towards the periphery of the tissue.

L18 ANSWER 85 OF 87 MEDLINE on STN
ACCESSION NUMBER: 91072958 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2254647
TITLE: A novel polyclonal antibody (CL-B1/29) for immunolocalization of transforming growth factor-beta 2 (TGF-beta 2) in adult mouse.
AUTHOR: Ksander G A; Gerhardt C O; Dasch J R; Ellingsworth L R
CORPORATE SOURCE: Department of Histology, Celtrix Laboratories, Palo Alto, California 94303.
SOURCE: The journal of histochemistry and cytochemistry : official journal of the Histochemistry Society, (1990 Dec) Vol. 38, No. 12, pp. 1831-40.
Journal code: 9815334. ISSN: 0022-1554.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199101
ENTRY DATE: Entered STN: 8 Mar 1991
Last Updated on STN: 6 Feb 1998
Entered Medline: 22 Jan 1991

AB A polyclonal antibody (CL-B1/29) raised against a synthetic peptide with an amino acid sequence identical to the first 29 N-terminal residues of bovine bone-derived transforming growth factor -beta 2 (TGF-beta 2) was characterized and used for immunolocalization of TGF-beta 2 in adult mice. Reduced staining of immunoblots and tissue after absorption of the antiserum with the immunizing peptide or with TGF-beta 2 but not with purified TGF-beta 1 demonstrated that the reagent is specific for TGF-beta 2, with little or no crossreactivity with TGF-beta 1. The immunolocalization of TGF-beta 2 was investigated in formalin-fixed, paraffin-embedded cultured cells and murine tissue. Specimens pre-digested with testicular hyaluronidase demonstrated immunostaining predominantly of extracellular connective tissue matrix, whereas specimens pre-digested with pronase E demonstrated primarily cytoplasmic staining. Immunoreactivity was widely distributed in connective tissue, muscle, adsorptive and secretory epithelia, especially of endocrine tissue, and neural tissue of adult mice.

L18 ANSWER 86 OF 87 MEDLINE on STN
ACCESSION NUMBER: 90344266 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1696488
TITLE: Transforming growth factors-beta 1 and beta 2 induce synthesis and accumulation of hyaluronate and chondroitin sulfate in vivo.
AUTHOR: Ogawa Y; Sawamura S J; Ksander G A; Armstrong R M; Pratt B M; McPherson J M
CORPORATE SOURCE: Celtrix Laboratories, Collagen Corporation, Palo Alto, California 94303.
SOURCE: Growth factors (Chur, Switzerland), (1990) Vol. 3, No. 1,

pp. 53-62.
Journal code: 9000468. ISSN: 0897-7194.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199009
ENTRY DATE: Entered STN: 26 Oct 1990
Last Updated on STN: 29 Jan 1996
Entered Medline: 20 Sep 1990

AB Subcutaneous implantation in rats of partially purified transforming growth factor-beta (TGF-beta) derived from bovine bone induced extensive development of connective tissue with associated edema. Subcutaneous injection of pure TGF-beta 1 or TGF-beta 2 also induced connective tissue deposition in mice and guinea pigs. Sustained release of TGF-beta 1 from mini-osmotic pumps implanted subcutaneously in mature guinea pigs promoted connective tissue deposition that encapsulated the pumps. Biochemical analyses of the connective tissue capsule demonstrated that TGF-beta 1 induced a dose-dependent accumulation of glycosaminoglycans (GAGs). The GAG/DNA ratio also increased as a function of the rate of TGF-beta 1 released, suggesting that the factor increased production of GAGs per cell. Cellulose acetate gel electrophoresis of the GAGs and hydrolysis with specific glycosidases revealed that the majority of GAGs consisted of hyaluronate and chondroitin sulfate. These results demonstrate that TGF-beta 1 and TGF-beta 2 stimulate the production of not only collagenous extracellular matrix components, but also dramatically increase the in vivo synthesis of hyaluronate and chondroitin sulfate.

L18 ANSWER 87 OF 87 MEDLINE on STN
ACCESSION NUMBER: 86213171 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3706785
TITLE: Changes in the extracellular matrix and glycosaminoglycan synthesis during the initiation of regeneration in adult newt forelimbs.
AUTHOR: Mescher A L; Munaim S I
SOURCE: The Anatomical record, (1986 Apr) Vol. 214, No. 4, pp. 424-31, 394-5.
Journal code: 0370540. ISSN: 0003-276X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198605
ENTRY DATE: Entered STN: 21 Mar 1990
Last Updated on STN: 6 Feb 1998
Entered Medline: 30 May 1986

AB The extracellular matrix (ECM) of the distal tissues in a newt limb stump is completely reorganized in the 2-3-week period following amputation. In view of numerous in vitro studies showing that extracellular material influences cellular migration and proliferation, it is likely that the changes in the limb's ECM are important activities in the process leading to regeneration of such limbs. Using biochemical, autoradiographic, and histochemical techniques we studied temporal and spatial differences in the synthesis of glycosaminoglycans (GAGs) during the early, nerve-dependent phase of limb regeneration. Hyaluronic acid synthesis began with the onset of tissue dedifferentiation, became maximal within 1 weeks, and continued throughout the period of active cell proliferation. Chondroitin sulfate synthesis began somewhat later, increased steadily, and reached very high levels during chondrogenesis. During the first 10 days after amputation, distributions of sulfated and nonsulfated GAGs were both uniform throughout dedifferentiating tissues, except for a heavier localization near the bone. Since nerves are necessary to promote the regenerative process, we examined the neural

influence on synthesis and accumulation of extracellular GAGs. Denervation decreased GAG production in all parts of the limb stump by approximately 50%. Newt dorsal root ganglia and brain-derived fibroblast growth factor each produced twofold stimulation of GAG synthesis in cultured 7-day regenerates. The latter effect was primarily on synthesis of hyaluronic acid. The results indicate that the trophic action of nerves on amphibian limb regeneration includes a positive influence on synthesis and extracellular accumulation of GAGs. Since the ECM exerts a major influence on cellular proliferation and migration, the effect of nerves on GAG metabolism may have considerable importance for growth and development of the early regenerate.

L18 ANSWER 47 OF 87 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1991:136145 CAPLUS
DOCUMENT NUMBER: 114:136145
TITLE: A novel polyclonal antibody (CL-B1/29) for immunolocalization of transforming growth factor-β2 (TGF-β2) in adult mouse
AUTHOR(S): Ksander, George A.; Gerhardt, Carolyn O.; Dasch, James R.; Ellingsworth, Larry R.
CORPORATE SOURCE: Dep. Histol., Celtrix Lab., Palo Alto, CA, 94303, USA
SOURCE: Journal of Histochemistry and Cytochemistry (1990), 38(12), 1831-40
CODEN: JHCYAS; ISSN: 0022-1554
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A polyclonal antibody (CL-B1/29) raised against a synthetic peptide with an amino acid sequence identical to the 1st 29 N-terminal residues of bovine bone-derived transforming growth factor -β2 (TGF-β2) was characterized and used for immunolocalization of TGF-β2 in adult mice. Reduced staining of immunoblots and tissue after absorption of the antiserum with the immunizing peptide or with TGF-β2 but not with purified TGF-β1 demonstrated that the reagent is specific for TGF-β2, with little or no crossreactivity with TGF-β1. The immunolocalization of TGF-β2 was investigated in formalin-fixed, paraffin-embedded cultured cells and murine tissue. Specimens pre-digested with testicular hyaluronidase demonstrated immunostaining predominantly of extracellular connective tissue matrix, whereas specimens predigested with pronase E demonstrated primarily cytoplasmic staining. Immunoreactivity was widely distributed in connective tissue, muscle, adsorptive and secretory epithelia, especially of endocrine tissue, and neural tissue of adult mice.

L18 ANSWER 48 OF 87 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1990:185867 CAPLUS
DOCUMENT NUMBER: 112:185867
TITLE: Biodegradable, osteogenic, bone graft substitute
INVENTOR(S): Brekke, John H.
PATENT ASSIGNEE(S): Osmed, Inc., USA
SOURCE: Brit. UK Pat. Appl., 32 pp.
CODEN: BAXXDU
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2215209	A1	19890920	GB 1988-11274	19880512
GB 2215209	B2	19920826		
JP 01232967	A2	19890918	JP 1988-174831	19880712
JP 2820415	B2	19981105		

PRIORITY APPLN. INFO.: US 1988-167370 A 19880314
AB A biodegradable device for facilitating healing of structural voids in bone comprises: (a) a biodegradable polymer constituting a hydroxy acid (e.g., polylactic or polyglycolic acid), (b) a chemotactic substance disposed throughout spaces in the polymer (e.g., hyaluronic acid, fibronectin, or collagen), and (c) a biol. active or therapeutic substance (e.g., bone morphogenetic protein or bone -derived growth factor). The device constituents are integrated into a single body member which, when implanted into a bone defect, has the capacity to restore functional architecture and mech. integrity, initiate osteoinduction and osteogenesis, and maintain the biol. processes of bone formation and remodeling while the host organism is simultaneously biodegrading the body member.

L18 ANSWER 49 OF 87 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1986:204289 CAPLUS
DOCUMENT NUMBER: 104:204289
TITLE: Changes in the extracellular matrix and glycosaminoglycan synthesis during the initiation of regeneration in adult newt forelimbs
AUTHOR(S): Mescher, Anthony L.; Munaim, Syeda Iffat
CORPORATE SOURCE: Anat. Sect., Indiana Univ., Bloomington, IN, 47405, USA
SOURCE: Anatomical Record (1986), 214(4), 424-31, 394-5
CODEN: ANREAK; ISSN: 0003-276X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The extracellular matrix (EDM) of the distal tissues in a newt (Notophthalmus viridescens) limb stump is completely reorganized in the 2-3-wk period following amputation. By using biochem., autoradiog., and histochem. techniques, temporal and spatial differences in the synthesis of glycosaminoglycans (GAGs) were studied during the early, nerve-dependent phase of limb regeneration. Hyaluronic acid synthesis began with the onset of tissue dedifferentiation, became maximal within 1 wk, and continued throughout the period of active cell proliferation. Chondroitin sulfate synthesis began somewhat later, increased steadily, and reached very high levels during chondrogenesis. During the 1st 10 days after amputation, distributions of sulfated and nonsulfated GAGs were both uniform throughout dedifferentiating tissues, except for a heavier localization near the bone. Since nerves are necessary to promote the regenerative process, the neural influence on synthesis and accumulation of extracellular GAGs was examined Denervation decreased GAG production in all parts of the limb stump by .apprx.50%. Newt dorsal root ganglia and brain-derived fibroblast growth factor each produced a 2-fold stimulation of GAG synthesis in cultured 7-day regenerates. The latter effect was primarily on synthesis of hyaluronic acid. Thus, the trophic action of nerves on amphibian limb regeneration includes a pos. influence on synthesis and extracellular accumulation of GAGs. Since the ECM exerts a major influence on cellular proliferation and migration, the effect of nerves on GAG metabolism may have considerable importance for growth and development of the early regenerate.

L18 ANSWER 50 OF 87 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1960:111701 CAPLUS
DOCUMENT NUMBER: 54:111701
ORIGINAL REFERENCE NO.: 54:21373i,21374a-d
TITLE: Quantitative studies on the production of acid mucopolysaccharides by replicate cell cultures of rat fibroblasts
AUTHOR(S): Morris, Charles Clark
CORPORATE SOURCE: Columbia Univ.
SOURCE: Annals of the New York Academy of Sciences (1960), 86, 876-915
CODEN: ANYAA9; ISSN: 0077-8923
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB cf. Grossfeld, et al., CA 51, 16649f. Formation of acid mucopolysaccharide (AMPS) by fibroblasts explanted from cranial bone was studied. AMPS production was most rapid during the 1st 24 hrs. after transferring the cells to fresh medium, then leveled off. However, deoxyribonucleic acid (DNA) synthesis was maximum in the 24-48-hr. period. Formation of both substances practically ceased after 96 hrs. A 7-fold increase in glucose concentration above the standard level of 0.1% or a 5-fold increase in CO2 tension did not influence AMPS production. When based on DNA content of cultures, maximum AMPS formation ranged from 40 to 50 μγ/cell/feeding period with initial rates of 1.1-1.6

μγ/cell/hr. No differences in rate were noted between recently isolated strains of cells and those isolated 3 years previously from a similar source. Glutamine at concns. of 10-300 γ/ml. did not stimulate growth of well-nourished cells, starved cells, or of cells rapidly depleted of endogenous reserves; in fact, it inhibited starved or depleted cells, possibly by competitive inhibition of an essential metabolic step. These cells did not normally require glutamine, but after adaptation to excess amts. it became an essential growth factor. The AMPS was composed predominantly of hyaluronic acid and 5-10% chondroitinsulfate which was not further identified. It was found that AMPS production and S35O4-- incorporation proceeded at different rates, which lends support to the concept that sulfation occurs at a late stage of AMPS synthesis. Histochem. studies revealed the presence of cytoplasmic granules staining with the HIO4-Schiff method which were unaffected by extraction with hot Me2CO or MeOH-CHCl3 or by digestion with hyaluronidase or salivary amylase. The number of these granules could not be correlated with the cell-bound AMPS content. The cells showed no metachromasia, but rather only basophilia with toluidine blue. This basophilia corresponded closely to the staining pattern with colloidal Fe.

L18 ANSWER 51 OF 87 MEDLINE on STN
ACCESSION NUMBER: 2006238297 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16306150
TITLE: The role of the hyaluronan receptor CD44 in mesenchymal stem cell migration in the extracellular matrix.
AUTHOR: Zhu Hui; Mitsuhashi Noboru; Klein Andrew; Barsky Lora W; Weinberg Kenneth; Barr Mark L; Demetriou Achilles; Wu Gordon D
CORPORATE SOURCE: Comprehensive Transplant Center, Department of Surgery, Cedars-Sinai Medical Center, 8700 Beverly Blvd., Los Angeles, California 90048, USA.
CONTRACT NUMBER: 1 R01AI05320 OA2 (NIAID)
SOURCE: Stem cells (Dayton, Ohio), (2006 Apr) Vol. 24, No. 4, pp. 928-35. Electronic Publication: 2005-11-23. Journal code: 9304532. ISSN: 1066-5099.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200606
ENTRY DATE: Entered STN: 29 Apr 2006
Last Updated on STN: 1 Jul 2006
Entered Medline: 30 Jun 2006

AB In a previous investigation, we demonstrated that mesenchymal stem cells (MSCs) actively migrated to cardiac allografts and contributed to graft fibrosis and, to a lesser extent, to myocardial regeneration. The cellular/molecular mechanism responsible for MSC migration, however, is poorly understood. This paper examines the role of CD44-hyaluronan interaction in MSC migration, using a rat MSC line Ap8c3 and mouse CD44-/- or CD44+/+ bone marrow stromal cells (BMSCs). Platelet-derived growth factor (PDGF) stimulation of MSC Ap8c3 cells significantly increased the levels of cell surface CD44 detected by flow cytometry. The CD44 standard isoform was predominantly expressed by Ap8c3 cells, accounting for 90% of the CD44 mRNA determined by quantitative real-time polymerase chain reaction. Mouse CD44-/- BMSCs bonded inefficiently to hyaluronic acid (HA), whereas CD44+/+ BMSC and MSC Ap8c3 adhered strongly to HA. Adhesions of MSC Ap8c3 cells to HA were suppressed by anti-CD44 antibody and by CD44 small interfering RNA (siRNA). HA coating of the migration chamber significantly promoted passage of CD44+/+ BMSC or Ap8c3 cells, but not CD44-/- BMSCs, through the insert membranes ($p < .01$). Migration of MSC Ap8c3 was significantly inhibited by anti-CD44 antibodies ($p < .01$) and to a lesser extent by CD44 siRNA ($p = .05$). The data indicate that

MSC Ap8c3 cells, in response to PDGF stimulation, express high levels of CD44 standard (CD44s) isoform, which facilitates cell migration through interaction with extracellular HA. Such a migratory mechanism could be critical for recruitment of MSCs into wound sites for the proposition of tissue regeneration, as well as for migration of fibroblast progenitors to allografts in the development of graft fibrosis.

L18 ANSWER 52 OF 87 MEDLINE on STN
ACCESSION NUMBER: 2005563160 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16238607
TITLE: Comparison of BMP-2 and -4 for rat mandibular bone regeneration at various doses.
AUTHOR: Arosarena O; Collins W
CORPORATE SOURCE: Division of Otolaryngology, Department of Surgery, University of Kentucky Medical Center, Lexington, 40536, USA.. oaaros2@pop.uky.edu
SOURCE: Orthodontics & craniofacial research, (2005 Nov) Vol. 8, No. 4, pp. 267-76.
Journal code: 101144387. ISSN: 1601-6335.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Dental Journals; Priority Journals
ENTRY MONTH: 200512
ENTRY DATE: Entered STN: 22 Oct 2005
Last Updated on STN: 23 Dec 2005
Entered Medline: 22 Dec 2005

AB OBJECTIVE: To compare mandibular bone regeneration with bone morphogenetic proteins-2 and -4 (BMP-2 and -4) at varying doses. STUDY DESIGN: Defects were created in the left hemi-mandibles of 82 Sprague-Dawley rats. The defects were filled with a hyaluronic acid polymer loaded with 0.01, 0.1, 1, or 10 microg of BMP-2 or -4. Control groups consisted of animals with unfilled defects, or with defects filled with the hyaluronic acid sponges loaded with growth factor dilution buffer. Animals were killed after 8 weeks, and the hemi-mandibles were analyzed histologically using stereologic techniques. RESULTS: Mandibles implanted with carriers containing 10 microg of BMP-2 or -4 differed significantly from controls in terms of new bone area ($p = 0.01$ and $p = 0.0001$, respectively). Marrow space development occurred in a dose-dependent fashion ($p < 0.0001$ for both growth factors), and this effect was more pronounced for BMP-2 at larger doses ($p < 0.0001$ at 1 and 10 microg doses). New bone areas and volumes did not differ significantly between the growth factors. While defects implanted with BMP-4 tended to have thicker cortical bone and more trabecular bone, at least partial defect bridging was achieved in a greater number of defects implanted with BMP-2 (47%) than with BMP-4 (35%). CONCLUSION: Although similar areas and volumes of new bone were induced with BMP-2 and -4, differences were noted in the quality of bone generated with each growth factor. The results indicate a threshold dose for acute administration between 1 and 10 mug BMP-2 for bony union in this model, and > or =10 microg for BMP-4. SIGNIFICANCE: These findings suggest that differences in bone growth factor osteogenic potential deserve further study and may have an impact on the translation of osteoinductive protein therapy into clinical practice.

L18 ANSWER 53 OF 87 MEDLINE on STN
ACCESSION NUMBER: 2004558664 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15531364
TITLE: Synergistic roles of BMP15 and GDF9 in the development and function of the oocyte-cumulus cell complex in mice: genetic evidence for an oocyte-granulosa cell regulatory loop.

AUTHOR: Su You-Qiang; Wu Xuemei; O'Brien Marilyn J; Pendola Frank L; Denegre James N; Matzuk Martin M; Eppig John J
CORPORATE SOURCE: The Jackson Laboratory, Bar Harbor, ME 04609, USA.
CONTRACT NUMBER: HD21970 (NICHD)
HD23839 (NICHD)
HD33438 (NICHD)
SOURCE: Developmental biology, (2004 Dec 1) Vol. 276, No. 1, pp. 64-73.
Journal code: 0372762. ISSN: 0012-1606.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200501
ENTRY DATE: Entered STN: 9 Nov 2004
Last Updated on STN: 14 Jan 2005
Entered Medline: 13 Jan 2005

AB Bone morphogenetic protein 15 (BMP15) and growth differentiation factor 9 (GDF9) are oocyte-specific growth factors that appear to play key roles in granulosa cell development and fertility in most mammalian species. We have evaluated the role(s) of these paracrine factors in the development and function of both the cumulus cells and oocytes by assessing cumulus expansion, oocyte maturation, fertilization, and preimplantation embryogenesis in Gdf9+/-Bmp15-/- [hereafter, double mutant (DM)] mice. We found that cumulus expansion, as well as the expression of hyaluronon synthase 2 (Has2) mRNA was impaired in DM oocyte-cumulus cell complexes. This aberrant cumulus expansion was not remedied by coculture with normal wild-type (WT) oocytes, indicating that the development and/or differentiation of cumulus cells in the DM, up to the stage of the preovulatory luteinizing hormone (LH) surge, is impaired. In addition, DM oocytes failed to enable FSH to induce cumulus expansion in WT oocytectomized (OOX) cumulus. Moreover, LH-induced oocyte meiotic resumption was significantly delayed in vivo, and this delayed resumption of meiosis was correlated with the reduced activation of mitogen-activated protein kinase (MAPK) in the cumulus cells, thus suggesting that GDF9 and BMP15 also regulate the function of cumulus cells after the preovulatory LH surge. Although spontaneous in vitro oocyte maturation occurred normally, oocyte fertilization and preimplantation embryogenesis were significantly altered in the DM, suggesting that the full complement of both GDF9 and BMP15 are essential for the development and function of oocytes. Because receptors for GDF9 and BMP15 have not yet been identified in mouse oocytes, the effects of the mutations in the Bmp15 and Gdf9 genes on oocyte development and functions must be produced indirectly by first affecting the granulosa cells and then the oocyte. Therefore, this study provides further evidence for the existence and functioning of an oocyte-granulosa cell regulatory loop.

L18 ANSWER 54 OF 87 MEDLINE on STN
ACCESSION NUMBER: 2004356434 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15259552
TITLE: Hyaluronan-based biomaterial (Hyaff-11) as scaffold to support mineralization of bone marrow stromal cells.
AUTHOR: Lisignoli G; Toneguzzi S; Zini N; Piacentini A; Cristino S; Tschon M; Grassi F; Fini M; Giardino R; Maraldi N M; Facchini A
CORPORATE SOURCE: Laboratorio di Immunologia e Genetica, Istituti Ortopedici Rizzoli, Bologna, Italy.
SOURCE: La Chirurgia degli organi di movimento, (2003 Oct-Dec) Vol. 88, No. 4, pp. 363-7.
Journal code: 0372573. ISSN: 0009-4749.
PUB. COUNTRY: Italy
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English; Italian

FILE SEGMENT: Priority Journals
ENTRY MONTH: 200501
ENTRY DATE: Entered STN: 21 Jul 2004
Last Updated on STN: 4 Jan 2005
Entered Medline: 3 Jan 2005

AB Various techniques are widely used to repair bone defects, association of hyaluronan-based biodegradable polymers (Hyaff-11) with bone marrow stromal cells (BMSC) promises to provide successful cell scaffolds for tissue-engineered repair of bone tissue. We evaluate in vitro and in vivo the potential of Hyaff-11 to facilitate mineralization of BMSC. Rat BMSC were seeded on Hyaff-11 and their differentiation were assessed at different time points. Osteogenic differentiation was investigated in vitro analysing the expression of alkaline phosphatase and osteocalcin. Mineralization of bone defects was evaluated also in vivo implanting Hyaff-11 scaffold combined with BMSC in large segmental radius defects. In vitro, we found a decrease expression of alkaline phosphatase and an increase of osteocalcin. In vivo, our data showed that mineralization was induced and basic fibroblast growth factor contributed to this process. These results provide a demonstration to therapeutic potential of Hyaff-11 as appropriate carrier vehicle for differentiation and mineralization of BMSC and for the repair of bone defects.

L18 ANSWER 55 OF 87 MEDLINE on STN
ACCESSION NUMBER: 2004206484 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15104217
TITLE: Control of angiogenesis by inhibitor of phospholipase A2.
AUTHOR: Chen Wenming; Li Lihong; Zhu Jiazhi; Liu Jinwei; Soria Jeannette; Soria Claudine; Yedgar Saul
CORPORATE SOURCE: Beijing Chaoyang Hospital, Capital University of Medical Sciences, Beijing 100020.. wenming_chen@yahoo.com
SOURCE: Chinese medical sciences journal = Chung-kuo i hsueh k'o hsueh tsa chih / Chinese Academy of Medical Sciences, (2004 Mar) Vol. 19, No. 1, pp. 6-12.
Journal code: 9112559. ISSN: 1001-9294.
PUB. COUNTRY: China
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200408
ENTRY DATE: Entered STN: 24 Apr 2004
Last Updated on STN: 14 Aug 2004
Entered Medline: 13 Aug 2004

AB OBJECTIVE: To investigate the potential effects of angiogenic process by secretory phospholipase A2 (sPLA2) inhibitor-HyPE (linking N-derivatized phosphatidyl-ethanolamine to hyaluronic acid) on human bone marrow endothelial cell line (HBME-1). METHODS: In order to examine the suppressing effects of HyPE on HBME-1 proliferation, migration, and capillary-like tube formation, HBME-1 were activated hy angiogenic factor, specifically by basic fibroblast growth factor (b-FGF), vascular endothelial growth factor (VEGF), and oncostatin M (OSM) (at a final concentration of 25, 20, and 2.5 ng/mL, respectively), then HBME-1 proliferation, migration, and tube formation were studied in the absence or presence of HyPE. HBME-1 tube formation was specially analyzed in fibrin gel. RESULTS: HyPE effectively inhibited HBME-1 proliferation and migration as a dose-dependent manner, whatever HBME-1 were grown in the control culture medium or stimulated with b-FGF, VEGF, or OSM. In fibrin, the formations of HBME-1 derived tube-like structures were enhanced by all angiogenic factors, but these were strongly suppressed by HyPE. CONCLUSIONS: The results support the involvement of sPLA2 in angiogenesis. It is proposed that sPLA2 inhibitor introduces a novel approach in the control of cancer development.

L18 ANSWER 56 OF 87 MEDLINE on STN
ACCESSION NUMBER: 2004147743 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15042541
TITLE: Gene expression profiling in glomeruli from human kidneys with diabetic nephropathy.
AUTHOR: Baelde Hans J; Eikmans Michael; Doran Peter P; Lappin David W P; de Heer Emile; Bruijn Jan A
CORPORATE SOURCE: Department of Pathology, Leiden University Medical Center, Leiden, The Netherlands.. j.j.baelde@lumc.nl
SOURCE: American journal of kidney diseases : the official journal of the National Kidney Foundation, (2004 Apr) Vol. 43, No. 4, pp. 636-50.
Journal code: 8110075. E-ISSN: 1523-6838.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200406
ENTRY DATE: Entered STN: 26 Mar 2004
Last Updated on STN: 17 Jun 2004
Entered Medline: 16 Jun 2004

AB BACKGROUND: Diabetic nephropathy (DN) is a frequent complication in patients with diabetes mellitus. To find improved intervention strategies in this disease, it is necessary to investigate the molecular mechanisms involved. To obtain more insight into processes that lead to DN, messenger RNA expression profiles of diabetic glomeruli and glomeruli from healthy individuals were compared. METHODS: Two morphologically normal kidneys and 2 kidneys from patients with DN were used for the study. Glomerular RNA was hybridized in duplicate on Human Genome U95Av2 Arrays (Affymetrix, Santa Clara, CA). Several transcripts were tested further in independent patient groups and at the protein level by immunohistochemistry. RESULTS: Ninety-six genes were upregulated in diabetic glomeruli, whereas 519 genes were downregulated. The list of overexpressed genes in DN includes aquaporin 1, calpain 3, hyaluronoglucosidase, and platelet/endothelial cell adhesion molecule. The list of downregulated genes includes bone morphogenetic protein 2, vascular endothelial growth factor (VEGF), fibroblast growth factor 1, insulin-like growth factor binding protein 2, and nephrin. A decrease in VEGF and nephrin could be validated at the protein level and also at the RNA level in renal biopsy specimens from 5 additional patients with diabetes. CONCLUSION: Results of oligonucleotide microarray analyses on control and diabetic glomeruli are presented and discussed in their relation to vascular damage, mesangial matrix expansion, proliferation, and proteinuria. Our findings suggest that progression of DN might result from diminished tissue repair capability.

L18 ANSWER 57 OF 87 MEDLINE on STN
ACCESSION NUMBER: 2003574625 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14653765
TITLE: Nutritional support for wound healing.
AUTHOR: MacKay Douglas; Miller Alan L
CORPORATE SOURCE: Thorne Research, Inc., PO Box 25, Dover, ID 83825, USA.. duffy@thorne.com
SOURCE: Alternative medicine review : a journal of clinical therapeutic, (2003 Nov) Vol. 8, No. 4, pp. 359-77. Ref: 126
Journal code: 9705340. ISSN: 1089-5159.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Consumer Health
ENTRY MONTH: 200402

ENTRY DATE: Entered STN: 16 Dec 2003
Last Updated on STN: 2 Mar 2004
Entered Medline: 27 Feb 2004

AB Healing of wounds, whether from accidental injury or surgical intervention, involves the activity of an intricate network of blood cells, tissue types, cytokines, and growth factors. This results in increased cellular activity, which causes an intensified metabolic demand for nutrients. Nutritional deficiencies can impede wound healing, and several nutritional factors required for wound repair may improve healing time and wound outcome. Vitamin A is required for epithelial and bone formation, cellular differentiation, and immune function. Vitamin C is necessary for collagen formation, proper immune function, and as a tissue antioxidant. Vitamin E is the major lipid-soluble antioxidant in the skin; however, the effect of vitamin E on surgical wounds is inconclusive. Bromelain reduces edema, bruising, pain, and healing time following trauma and surgical procedures. Glucosamine appears to be the rate-limiting substrate for hyaluronic acid production in the wound. Adequate dietary protein is absolutely essential for proper wound healing, and tissue levels of the amino acids arginine and glutamine may influence wound repair and immune function. The botanical medicines Centella asiatica and Aloe vera have been used for decades, both topically and internally, to enhance wound repair, and scientific studies are now beginning to validate efficacy and explore mechanisms of action for these botanicals. To promote wound healing in the shortest time possible, with minimal pain, discomfort, and scarring to the patient, it is important to explore nutritional and botanical influences on wound outcome.

L18 ANSWER 58 OF 87 MEDLINE on STN
ACCESSION NUMBER: 2003477049 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14555276
TITLE: Hyaluronic acid reverses the abnormal synthetic activity of human osteoarthritic subchondral bone osteoblasts.
AUTHOR: Lajeunesse Daniel; Delalandre Aline; Martel-Pelletier Johanne; Pelletier Jean Pierre
CORPORATE SOURCE: Unite de recherche en Arthrose, Centre de recherche du Centre Hospitalier de I'Universite de Montreal, Montreal, Quebec H2L 4M1, Canada.. lajeunda@jonction.net
SOURCE: Bone, (2003 Oct) Vol. 33, No. 4, pp. 703-10. Journal code: 8504048. ISSN: 8756-3282.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200407
ENTRY DATE: Entered STN: 15 Oct 2003
Last Updated on STN: 7 Jul 2004
Entered Medline: 6 Jul 2004

AB The underlying mechanisms responsible for both cartilage loss and subchondral bone changes in osteoarthritis (OA) remain unknown. It is becoming recognized that the extracellular matrix influences the metabolism of cells both in vivo and in vitro and can modify their responses to external stimuli. Indeed, the glycosaminoglycan/proteoglycan matrix is of major importance for the proliferation and/or differentiation of a number of cells. Here, we determined the potential role of hyaluronic acid (HA) of increasing molecular weight (MW) to alter the expression of metabolic markers and cytokine production by human osteoarthritic (OA) subchondral osteoblasts (Ob). Both 1,25(OH)(2)D(3)-induced alkaline phosphatase activity (ALPase) and osteocalcin release were increased in OA Ob when compared to normal. HA reduced osteocalcin release in OA Ob at MW of 300 and above, whereas HA failed to significantly modify ALPase. Parathyroid hormone (PTH) stimulated cyclic AMP (cAMP) formation by OA Ob. HA had a biphasic effect on this PTH-dependent activity, totally inhibiting cAMP formation at MW of

300 and 800. HA of increasing MW progressively reduced the levels of Prostaglandin E(2) (PGE(2)) and interleukin-6 (IL-6) produced by OA Ob. Interestingly, urokinase plasminogen activator (uPA) and and PA inhibitor-1 (PAI-1) levels were not significantly affected by HA of increasing MW; however, the PAI-1 to uPA ratio showed a slight, yet nonsignificant increase. Surprisingly, uPA activity was increased in OA Ob under the same conditions. Last, HA had no effect on the production of insulin-like growth factor-1 by these cells. Our data suggest that high MW HA can modify cellular parameters in OA Ob that are increased when compared to normal. The effect of HA on inflammatory mediators, such as PGE(2) and IL-6, and on uPA activity is more striking at higher MW as well. Taken together, these results could suggest that HA of increasing MW has positive effects on OA Ob by modifying their biological synthetic capacities.

L18 ANSWER 59 OF 87 MEDLINE on STN
ACCESSION NUMBER: 2003336960 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12689941
TITLE: The role of autocrine FGF-2 in the distinctive bone marrow fibrosis of hairy-cell leukemia (HCL).
AUTHOR: Aziz Khalil A; Till Kathleen J; Chen Haijuan; Slupsky Joseph R; Campbell Fiona; Cawley John C; Zuzel Mirko
CORPORATE SOURCE: Department of Haematology, University of Liverpool, Liverpool, United Kingdom.
SOURCE: Blood, (2003 Aug 1) Vol. 102, No. 3, pp. 1051-6. Electronic Publication: 2003-04-10. Journal code: 7603509. ISSN: 0006-4971.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200309
ENTRY DATE: Entered STN: 19 Jul 2003
Last Updated on STN: 23 Sep 2003
Entered Medline: 22 Sep 2003

AB Bone marrow (BM) fibrosis is a central diagnostic and pathogenetic feature of hairy-cell leukemia (HCL). It is known that fibronectin (FN) produced and assembled by the malignant hairy cells (HCs) themselves is a major component of this fibrosis. It is also known that FN production is greatly enhanced by adhesion of HCs to hyaluronan (HA) via CD44. The aim of the present study was to establish the roles of fibrogenic autocrine cytokines (fibroblast growth factor -2 [FGF-2] and transforming growth factor beta [TGFbeta]) and of different isoforms of CD44 in this FN production. We show that HC adhesion to HA stimulates FGF-2, but not TGFbeta, production and that HCs possess FGF-2 receptor. In a range of experiments, FN production was greatly reduced by blocking FGF-2 but not TGFbeta. Moreover FN, but not FGF-2, secretion was blocked by down-regulation of the v3 isoform of CD44 and by addition of heparitinase. These results show that autocrine FGF-2 secreted by HCs is the principal cytokine responsible for FN production by these cells when cultured on HA. The central role of FGF-2 in the pathogenesis of the BM fibrosis of HCL was supported by our immunohistochemical demonstration of large amounts of this cytokine in fibrotic BM but not in HCL spleen where there is no fibrosis. As regards CD44 isoforms, the present work demonstrates that CD44v3 is essential for providing the heparan sulfate necessary for HC stimulation by FGF-2, whereas the signal for production of the cytokine was provided by HA binding to CD44H, the standard hematopoietic form of the molecule.

L18 ANSWER 60 OF 87 MEDLINE on STN
ACCESSION NUMBER: 2003291063 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12818643
TITLE: Local roles of TGF-beta superfamily members in the control

of ovarian follicle development.
AUTHOR: Knight Philip G; Glister Claire
CORPORATE SOURCE: School of Animal and Microbial Sciences, University of Reading, Whiteknights, Reading RG6 6AJ, UK.. p.g.knight@reading.ac.uk
SOURCE: Animal reproduction science, (2003 Oct 15) Vol. 78, No. 3-4, pp. 165-83. Ref: 96
Journal code: 7807205. ISSN: 0378-4320.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200310
ENTRY DATE: Entered STN: 24 Jun 2003
Last Updated on STN: 24 Oct 2003
Entered Medline: 23 Oct 2003

AB Members of the transforming growth factor-beta (TGF-beta) superfamily have wide-ranging influences on many tissue and organ systems including the ovary. Two recently discovered TGF-beta superfamily members, growth/differentiation factor-9 (GDF-9) and bone morphogenetic protein-15 (BMP-15; also designated as GDF-9B) are expressed in an oocyte-specific manner from a very early stage and play a key role in promoting follicle growth beyond the primary stage. Follicle growth to the small antral stage does not require gonadotrophins but appears to be driven by local autocrine/paracrine signals from both somatic cell types (granulosa and theca) and from the oocyte. TGF-beta superfamily members expressed by follicular cells and implicated in this phase of follicle development include TGF-beta, activin, GDF-9/9B and several BMPs. Acquisition of follicle-stimulating hormone (FSH) responsiveness is a pre-requisite for growth beyond the small antral stage and evidence indicates an autocrine role for granulosa-derived activin in promoting granulosa cell proliferation, FSH receptor expression and aromatase activity. Indeed, some of the effects of FSH on granulosa cells may be mediated by endogenous activin. At the same time, activin may act on theca cells to attenuate luteinizing hormone (LH)-dependent androgen production in small to medium-size antral follicles. Dominant follicle selection appears to depend on differential FSH sensitivity amongst a growing cohort of small antral follicles. Activin may contribute to this selection process by sensitizing those follicles with the highest "activin tone" to FSH. Production of inhibin, like oestradiol, increases in selected dominant follicles, in an FSH- and insulin-like growth factor-dependent manner and may exert a paracrine action on theca cells to upregulate LH-induced secretion of androgen, an essential requirement for further oestradiol secretion by the pre-ovulatory follicle. Like activin, BMP-4 and -7 (mostly from theca), and BMP-6 (mostly from oocyte), can enhance oestradiol and inhibin secretion by bovine granulosa cells while suppressing progesterone secretion; this suggests a functional role in delaying follicle luteinization and/or atresia. Follistatin, on the other hand, may favor luteinization and/or atresia by bio-neutralizing intrafollicular activin and BMPs. Activin receptors are expressed by the oocyte and activin may have a further intrafollicular role in the terminal stages of follicle differentiation to promote oocyte maturation and developmental competence. In a reciprocal manner, oocyte-derived GDF-9/9B may act on the surrounding cumulus granulosa cells to attenuate oestradiol output and promote progesterone and hyaluronic acid production, mucification and cumulus expansion.

L18 ANSWER 61 OF 87 MEDLINE on STN
ACCESSION NUMBER: 2003176254 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12694247
TITLE: Hyaluronan, a major non-protein glycosaminoglycan component of the extracellular matrix in human bone marrow, mediates

dexamethasone resistance in multiple myeloma.
AUTHOR: Vincent Thierry; Molina Laurence; Espert Lucile; Mechti Nadir
CORPORATE SOURCE: INSERM Unite U475 and UMR-CNRS5094, Montpellier, and Laboratoire d'Hematologie, Hopital St-Eloi, Montpellier, France.
SOURCE: British journal of haematology, (2003 Apr) Vol. 121, No. 2, pp. 259-69.
Journal code: 0372544. ISSN: 0007-1048.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200305
ENTRY DATE: Entered STN: 17 Apr 2003
Last Updated on STN: 28 May 2003
Entered Medline: 27 May 2003

AB Originating from a post-switch memory B cell or plasma cell compartment in peripheral lymphoid tissues, malignant multiple myeloma (MM) cells accumulate in the bone marrow of patients with MM. In this favourable microenvironment, their growth and survival are dependent upon both soluble factors and physical cell-to-cell and cell-to-extracellular-matrix contacts. In this study, hyaluronan (HA), a major non-protein glycosaminoglycan component of the extracellular matrix in mammalian bone marrow, acted as a survival factor against dexamethasone (Dex)-induced apoptosis in MM cell lines. These effects were mediated through an interleukin 6 (IL-6) autocrine pathway, involving signal transducers and activators of transcription-3 phosphorylation on IL-6-dependent XG-1 and XG-6 cell lines. HA promoted accumulation of IL-6 in the culture medium without affecting IL-6 gene expression, suggesting that HA protects, stabilizes and concentrates IL-6 close to its site of secretion, thus favouring its autocrine activity. In contrast, in the IL-6-independent RPMI8226 cell line, HA survival effect was mediated through a gp80-IL-6 receptor-independent pathway, resulting in the upregulation of Bcl-2 anti-apoptotic protein expression and nuclear factor-kappaB activation. Taken together, these data suggest that HA antagonizes Dex-induced apoptosis of MM cells by favouring the autocrine activity of different cytokines or growth factors. As HA is a major component of the bone marrow extracellular matrix, these findings support the idea that HA could play a major role in the survival of MM cells in vivo, and could explain why MM cells accumulate in the bone marrow of patients with MM and escape conventional chemotherapy.

L18 ANSWER 62 OF 87 MEDLINE on STN
ACCESSION NUMBER: 2002352509 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12095629
TITLE: Control of capillary formation by membrane-anchored extracellular inhibitor of phospholipase A(2).
AUTHOR: Chen W M; Soria J; Soria C; Krimsky M; Yedgar S
CORPORATE SOURCE: INSERM - EMI 99-12, Hotel Dieu, Paris, France.
SOURCE: FEBS letters, (2002 Jul 3) Vol. 522, No. 1-3, pp. 113-8.
Journal code: 0155157. ISSN: 0014-5793.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200208
ENTRY DATE: Entered STN: 4 Jul 2002
Last Updated on STN: 15 Aug 2002
Entered Medline: 14 Aug 2002

AB Secretory phospholipase A(2) (sPLA(2)) has been reported to be involved in cell proliferation in general and in endothelial cell migration, processes required for capillary formation. Subsequently, we examined the potential

control of angiogenesis by sPLA(2) inhibition, using a cell-impermeable sPLA(2) inhibitor composed of N-derivatized phosphatidyl-ethanolamine linked to hyaluronic acid. This inhibitor effectively inhibits the proliferation and migration of human bone marrow endothelial cells in a dose-dependent manner, and suppresses capillary formation induced by growth factors involved in vascularization of tumors and of atherosclerotic plaques. It is proposed that sPLA(2) inhibition introduces a novel approach in the control of cancer development and atherosclerosis.

L18 ANSWER 63 OF 87 MEDLINE on STN
ACCESSION NUMBER: 2002066655 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11791907
TITLE: Osteogenesis of large segmental radius defects enhanced by basic fibroblast growth factor activated bone marrow stromal cells grown on non-woven hyaluronic acid-based polymer scaffold.
AUTHOR: Lisignoli G; Fini M; Giavaresi G; Nicoli Aldini N; Toneguzzi S; Facchini A
CORPORATE SOURCE: Laboratorio di Immunologia e Genetica, Istituti Ortopedici Rizzoli, Bologna, Italy.
SOURCE: Biomaterials, (2002 Feb) Vol. 23, No. 4, pp. 1043-51. Journal code: 8100316. ISSN: 0142-9612.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200207
ENTRY DATE: Entered STN: 25 Jan 2002
Last Updated on STN: 25 Jul 2002
Entered Medline: 24 Jul 2002
AB Osteogenesis of large segmental radius defects in a rat model was studied by implanting a biodegradable non-woven hyaluronic acid-based polymer scaffold (Hyaff 11) alone or in combination with bone marrow stromal cells (BMSCs). These cells had been previously grown in vitro in mineralising medium either supplemented with basic fibroblast growth factor (bFGF) or unsupplemented. The healing of bone defects was evaluated at 40, 80, 160 and 200 days and the repair process investigated by radiographic, histomorphometric (assessment of new bone growth and lamellar bone) and histological analyses (toluidine blue and von Kossa staining). Mineralisation of bone defects occurred in the presence of the Hyaff 11 scaffold alone or when combined with BMSCs grown with or without bFGF, but each process had a different timing. In particular, bFGF significantly induced mineralisation from day 40, whereas 160 days were necessary for direct evidence that a similar process was developing under the other two conditions tested (scaffold alone or with BMSCs). Radiographic score, new bone growth and lamellar bone percentage were highly correlated. The present outcomes were further confirmed by toluidine blue and von Kossa staining. According to these in vivo findings, the Hyaff 11 scaffold is an appropriate carrier vehicle for the repair of bone defects; additionally, it can significantly accelerate bone mineralisation in combination with BMSCs and bFGF.

L18 ANSWER 64 OF 87 MEDLINE on STN
ACCESSION NUMBER: 2002016690 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11432589
TITLE: Basic fibroblast growth factor enhances in vitro mineralization of rat bone marrow stromal cells grown on non-woven hyaluronic acid based polymer scaffold.
AUTHOR: Lisignoli G; Zini N; Remiddi G; Piacentini A; Puggioli A; Trimarchi C; Fini M; Maraldi N M; Facchini A
CORPORATE SOURCE: Laboratorio di Immunologia e Genetica. Istituti Ortopedici

Rizzoli, Bologna, Italy.
SOURCE: Biomaterials, (2001 Aug) Vol. 22, No. 15, pp. 2095-105. Journal code: 8100316. ISSN: 0142-9612.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 21 Jan 2002
Last Updated on STN: 21 Jan 2002
Entered Medline: 7 Dec 2001

AB A biodegradable non-woven hyaluronic acid polymer scaffold (Hyaff 11) was analysed in vitro as a carrier vehicle for differentiation and mineralization of rat bone marrow stromal cells (BMSC). BMSC were grown on Hyaff 11 in a mineralizing medium in the presence/absence of basic fibroblast growth factor (bFGF). Osteoblastic differentiation was investigated by light and electron microscopy analysing the expression of osteogenic markers: calcium, alkaline phosphatase (AP), osteopontin (OP), bone sialoprotein (BSP) and collagen type 1. We also measured proliferation, AP activity and mRNA expression of AP and osteocalcin (OC). Electron microscopy and Toluidine-blue staining demonstrated that bFGF accelerated (day 20 vs. day 40) and increased mineralization. With bFGF, calcium, OP and BSP were strongly enhanced at day 40, whereas AP decreased. Our in vitro results demonstrate that Hyaff 11 is a useful vehicle for growth, differentiation and mineralization of rat BMSC, and that it permits bone development.

L18 ANSWER 65 OF 87 MEDLINE on STN
ACCESSION NUMBER: 2001462025 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11506726
TITLE: Tissue-engineered fabrication of an osteochondral composite graft using rat bone marrow-derived mesenchymal stem cells.
AUTHOR: Gao J; Dennis J E; Solchaga L A; Awadallah A S; Goldberg V M; Caplan A I
CORPORATE SOURCE: Skeletal Research Center, Department of Biology, Case Western Reserve University, Cleveland, Ohio 44106, USA.
SOURCE: Tissue engineering, (2001 Aug) Vol. 7, No. 4, pp. 363-71. Journal code: 9505538. ISSN: 1076-3279.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20 Aug 2001
Last Updated on STN: 22 Jan 2002
Entered Medline: 4 Dec 2001

AB This study tested the tissue engineering hypothesis that construction of an osteochondral composite graft could be accomplished using multipotent progenitor cells and phenotype-specific biomaterials. Rat bone marrow-derived mesenchymal stem cells (MSCs) were culture-expanded and separately stimulated with transforming growth factor -beta1 (TGF-beta1) for chondrogenic differentiation or with an osteogenic supplement (OS). MSCs exposed to TGF-beta1 were loaded into a sponge composed of a hyaluronan derivative (HYAF-11) for the construction of the cartilage component of the composite graft, and MSCs exposed to OS were loaded into a porous calcium phosphate ceramic component for bone formation. Cell-loaded HYAFF-11 sponge and ceramic were joined together with fibrin sealant, Tisseel, to form a composite osteochondral graft, which was then implanted into a subcutaneous pocket in syngeneic rats. Specimens were harvested at 3 and 6 weeks after implantation, examined with histology for morphologic features, and stained immunohistochemically for type I, II, and X collagen. The two-component composite graft remained as an integrated

unit after in vivo implantation and histologic processing. Fibrocartilage was observed in the sponge, and bone was detected in the ceramic component. Observations with polarized light indicated continuity of collagen fibers between the ceramic and HYAFF-11 components in the 6-week specimens. Type I collagen was identified in the neo-tissue in both sponge and ceramic, and type II collagen in the fibrocartilage, especially the pericellular matrix of cells in the sponge. These data suggest that the construction of a tissue-engineered composite osteochondral graft is possible with MSCs and different biomaterials and bioactive factors that support either chondrogenic or osteogenic differentiation.

L18 ANSWER 66 OF 87 MEDLINE on STN
ACCESSION NUMBER: 2001401329 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11453237
TITLE: In vitro comparison of bioabsorbable and non-resorbable membranes in bone regeneration.
AUTHOR: Marinucci L; Lilli C; Baroni T; Becchetti E; Belcastro S; Balducci C; Locci P
CORPORATE SOURCE: Department of Experimental Medicine and Biochemistry, University of Perugia, Italy.
SOURCE: Journal of periodontology, (2001 Jun) Vol. 72, No. 6, pp. 753-9.
Journal code: 8000345. ISSN: 0022-3492.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Dental Journals; Priority Journals
ENTRY MONTH: 200109
ENTRY DATE: Entered STN: 1 Oct 2001
Last Updated on STN: 1 Oct 2001
Entered Medline: 27 Sep 2001

AB BACKGROUND: Barrier membranes are used to prevent down-growth of the oral mucosa along the root surface and to allow alveolar bone regeneration in guided tissue regeneration. Several studies have demonstrated bone regenerates in the presence of bioabsorbable and non-resorbable membranes, but no studies have compared multiple bioabsorbable barriers to one another and to non-resorbable barriers. This study evaluated the in vitro influence of bioabsorbable and non-resorbable membranes on specific parameters of human osteoblast activity. METHODS: Human osteoblasts were cultured on bioabsorbable membranes made of collagen, hyaluronic acid, and poly DL-lactide, and the most common non-resorbable membrane which is made of expanded polytetrafluoroethylene (ePTFE). The osteoblasts were cultured in vitro for 24 hours on barrier membranes in the presence of 3H-thymidine and 3H-proline to study cell proliferation and collagen synthesis. Transforming growth factor-beta1 (TGF-beta1) secretion was evaluated in conditioned media using an ELISA kit. RESULTS: The results showed that collagen and poly DL-lactide stimulated DNA synthesis more than ePTFE and hyaluronic acid. All bioabsorbable membranes significantly increased collagen synthesis and alkaline phosphatase activity. Collagen and hyaluronic acid increased secretion of TGF-beta1, a growth factor involved in bone remodeling. CONCLUSIONS: These data suggest bioabsorbable membranes, particularly collagen and hyaluronic acid, may promote bone regeneration through their activity on osteoblasts.

L18 ANSWER 27 OF 87 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:513233 CAPLUS
DOCUMENT NUMBER: 136:268062
TITLE: In vitro comparison of bioabsorbable and non-resorbable membranes in bone regeneration
AUTHOR(S): Marinucci, Lorella; Lilli, Cinzia; Baroni, Tiziano; Becchetti, Ennio; Belcastro, Salvatore; Balducci, Chiara; Locci, Paola
CORPORATE SOURCE: Department of Experimental Medicine and Biochemistry, University of Perugia, Perugia, Italy
SOURCE: Journal of Periodontology (2001), 72(6), 753-759
CODEN: JOPRAJ; ISSN: 0022-3492
PUBLISHER: American Academy of Periodontology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Barrier membranes are used to prevent down-growth of the oral mucosa along the root surface and to allow alveolar bone regeneration in guided tissue regeneration. Several studies have demonstrated bone regenerates in the presence of bioabsorbable and non-resorbable membranes, but no studies have compared multiple bioabsorbable barriers to one another and to non-resorbable barriers. This study evaluated the in vitro influence of bioabsorbable and non-resorbable membranes on specific parameters of human osteoblast activity. Human osteoblasts were cultured on bioabsorbable membranes made of collagen, hyaluronic acid, and poly(DL-lactide), and the most common non-resorbable membrane which is made of expanded polytetrafluoroethylene (ePTFE). The osteoblasts were cultured in vitro for 24 h on barrier membranes in the presence of 3H-thymidine and 3H-proline to study cell proliferation and collagen synthesis. Transforming growth factor-β1 (TGF-β1) secretion was evaluated in conditioned media using an ELISA kit. Collagen and poly(DL-lactide) stimulated DNA synthesis more than ePTFE and hyaluronic acid. All bioabsorbable membranes significantly increased collagen synthesis and alkaline phosphatase activity. Collagen and hyaluronic acid increased secretion of TGF-β1, a growth factor involved in bone remodeling. These data suggest bioabsorbable membranes, particularly collagen and hyaluronic acid, may promote bone regeneration through their activity on osteoblasts.
REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 28 OF 87 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:396014 CAPLUS
DOCUMENT NUMBER: 135:132737
TITLE: Synergistic roles of bone morphogenetic protein 15 and growth differentiation factor 9 in ovarian function
AUTHOR(S): Yan, Changning; Wang, Pei; DeMayo, Janet; DeMayo, Francesco J.; Elvin, Julia A.; Carino, Cecilia; Prasad, Sarvamangala V.; Skinner, Sheri S.; Dunbar, Bonnie S.; Dube, Jennifer L.; Celeste, Anthony J.; Matzuk, Martin M.
CORPORATE SOURCE: Department of Pathology, Baylor College of Medicine, Houston, TX, 77030, USA
SOURCE: Molecular Endocrinology (2001), 15(6), 854-866
CODEN: MOENEN; ISSN: 0888-8809
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Knockout mouse technol. has been used over the last decade to define the essential roles of ovarian-expressed genes and uncover genetic interactions. In particular, the authors have used this technol. to study the function of multiple members of the transforming growth

factor-β superfamily including inhibins, activins, and growth differentiation factor 9 (GDF-9 or Gdf9). Knockout mice lacking GDF-9 are infertile due to a block in folliculogenesis at the primary follicle stage. In addition, recombinant GDF-9 regulates multiple cumulus granulosa cell functions in the periovulatory period including hyaluronic acid synthesis and cumulus expansion. The authors have also cloned an oocyte-specific homolog of GDF-9 from mice and humans, which is termed bone morphogenetic protein 15 (BMP-15 or Bmp15). To define the function of BMP-15 in mice, the authors generated embryonic stem cells and knockout mice, which have a null mutation in this X-linked gene. Male chimeric and Bmp15 null mice are normal and fertile. In contrast to Bmp15 null males and Gdf9 knockout females, Bmp15 null females (Bmp15-/-) are subfertile and usually have minimal ovarian histopathol. defects, but demonstrate decreased ovulation and fertilization rates. To further decipher possible direct or indirect genetic interactions between GDF-9 and BMP-15, the authors have generated double mutant mice lacking one or both alleles of these related homologs. Double homozygote females (Bmp15-/-Gdf9-/-) display oocyte loss and cysts and resemble Gdf9-/- mutants. In contrast, Bmp15-/-Gdf9+/- female mice have more severe fertility defects than Bmp15-/- females, which appear to be due to abnormalities in ovarian folliculogenesis, cumulus cell physiol., and fertilization. Thus, the dosage of intact Bmp15 and Gdf9 alleles directly influences the destiny of the oocyte during folliculogenesis and in the periovulatory period. These studies have important implications for human fertility control and the maintenance of fertility and normal ovarian physiol.

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 29 OF 87 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:371365 CAPLUS
DOCUMENT NUMBER: 134:357624
TITLE: Bone prosthetic materials comprising calcium phosphate and bone formation inducers
INVENTOR(S): Irie, Hiroyuki
PATENT ASSIGNEE(S): Olympus Optical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 4 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001137328	A2	20010522	JP 1999-321294	19991111

PRIORITY APPLN. INFO.: JP 1999-321294 19991111

AB This invention relates to bone fillers comprising (1) multiporous β-tricalcium phosphate with porosity of 60-80 % and pore diameter 50-1000 μm and (2) bone-formation promoters selected from the group consisting of atelocollagens, hyaluronic acid, fibrin pastes, gelatins, and growth factors. A freeze-dried powder contained porous β-tricalcium phosphate and recombinant bone morphogenetic protein.

L18 ANSWER 30 OF 87 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:344084 CAPLUS
DOCUMENT NUMBER: 136:68427
TITLE: Differentiation stages of eosinophils characterized by hyaluronic acid binding via CD44 and responsiveness to stimuli
AUTHOR(S): Watanabe, Yoshiya; Hashizume, Minoru; Kataoka, Sayo; Hamaguchi, Emi; Morimoto, Norihito; Tsuru, Shinobu; Katoh, Shigeki; Miyake, Kensuke; Matsushima, Kouji;

AUTHOR(S): Tominaga, Mari; Kurashige, Takanobu; Fujimoto, Shigeyoshi; Kincade, Paul W.; Tominaga, Akira
CORPORATE SOURCE: Department of Medical Biology, Kochi Medical School, Nankoku City, Japan
SOURCE: DNA and Cell Biology (2001), 20(4), 189-202
CODEN: DCEBE8; ISSN: 1044-5498
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To characterize interleukin (IL)-5-induced eosinophils, we examined the expression of CD44, very late antigen (VLA)-4, and the IL-5 receptor α chain, as well as the levels of eosinophil peroxidase and the generation of superoxide. Eosinophils were prepared from IL-5-transgenic mice, then characterized using electron microscopy to determine their responses to stimuli. Whereas CD44 densities remained almost constant, the level of VLA-4 increased in parallel with eosinophil maturation. Although a subset of IL-5-induced eosinophils with high side scatter recovered from bone marrow and rare ones found in blood recognized hyaluronic acid (HA), most did not have this property. Bone marrow eosinophils with high side scatter and lower d. contained eosinophil peroxidase, not only in granules, but also in membranous structures for 30% of this population. This population developed HA-binding ability in response to IL-3, IL-4, IL-5, granulocyte-macrophage colony-stimulating factor, macrophage inflammatory protein (MIP)-2, monocyte chemotactic protein (MCP)-1, eotaxin, nerve growth factor (NGF), and opsonized zymosan (OZ). Peripheral blood eosinophils acquired HA-binding ability in response to the same stimuli, but their responses were less than those of bone marrow eosinophils with high levels of side scatter. However, splenic eosinophils did not respond to these stimuli. Although peripheral blood eosinophils did not proliferate when stimulated by IL-5, these were the only cells that released eosinophil peroxidase in response to IL-4, MIP-2, MCP-1, eotaxin, NGF, and OZ. With the exception of a subset of bone marrow eosinophils, the ability to acquire HA binding, but not the ability to generate superoxide, correlated with eosinophil peroxidase activity and major basic protein accumulation in the granules of maturing cells.

REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 31 OF 87 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:294955 CAPLUS
DOCUMENT NUMBER: 134:290753
TITLE: Method of promoting bone growth with hyaluronic acid and growth factors
INVENTOR(S): Radomsky, Michael
PATENT ASSIGNEE(S): Orquest, Inc., USA
SOURCE: U.S., 11 pp., Cont.-in-part of U.S. 5,942,499.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6221854	B1	20010424	US 1999-360543	19990726
US 5942499	A	19990824	US 1997-811971	19970305
CA 2378328	AA	20010201	CA 2000-2378328	20000726
WO 2001007056	A1	20010201	WO 2000-US20373	20000726
WO 2001007056	C2	20020725		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,

HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1198235	A1	20020424	EP 2000-950736	20000726
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003505422	T2	20030212	JP 2001-511940	20000726
NZ 516097	A	20040227	NZ 2000-516097	20000726
AU 777328	B2	20041014	AU 2000-63797	20000726
US 2001014664	A1	20010816	US 2001-825688	20010403
US 6703377	B2	20040309		
US 2004176295	A1	20040909	US 2004-796441	20040308
AU 2005200146	A1	20050210	AU 2005-200146	20050113

PRIORITY APPLN. INFO.:

US 1996-611690	B2	19960305
US 1997-811971	A2	19970305
US 1999-360543	A	19990726
WO 2000-US20373	W	20000726
US 2001-825688	A1	20010403

AB A bone growth-promoting composition is provided comprising hyaluronic acid and a growth factor. The composition has a viscosity and biodegradability sufficient to persist at an intra-articular site of desired bone growth for a period of time sufficient to promote the bone growth. Preferably hyaluronic acid is used in a composition range of 0.1-4% by weight and preferred growth factor is bFGF, present in a concentration range of about 10#-6 to 100 mg/mL.

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 32 OF 87 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:78247 CAPLUS
DOCUMENT NUMBER: 134:125970
TITLE: Method of promoting bone growth with hyaluronic acid and growth factors
INVENTOR(S): Randomsky, Michael
PATENT ASSIGNEE(S): Orquest, Inc., USA
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001007056	A1	20010201	WO 2000-US20373	20000726
WO 2001007056	C2	20020725		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6221854	B1	20010424	US 1999-360543	19990726
CA 2378328	AA	20010201	CA 2000-2378328	20000726
EP 1198235	A1	20020424	EP 2000-950736	20000726

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL

JP 2003505422	T2	20030212	JP 2001-511940	20000726
NZ 516097	A	20040227	NZ 2000-516097	20000726
AU 777328	B2	20041014	AU 2000-63797	20000726
AU 2005200146	A1	20050210	AU 2005-200146	20050113
PRIORITY APPLN. INFO.:			US 1999-360543 A	19990726
			US 1996-611690 B2	19960305
			US 1997-811971 A2	19970305
			WO 2000-US20373 W	20000726

AB A bone growth-promoting composition is provided comprising hyaluronic acid and a growth factor. The composition has a viscosity and biodegradability sufficient to persist at an intra-articular site of desired bone growth for a period of time sufficient to promote the bone growth. Preferably hyaluronic acid is used in a composition range of 0.1-4 % by weight and preferred growth factor is bFGF, present in a concentration range of about 10-6 to 100 mg/mL.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 33 OF 87 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:537943 CAPLUS
DOCUMENT NUMBER: 131:161648
TITLE: Method of promoting bone growth with hyaluronic acid and growth factors
INVENTOR(S): Radomsky, Michael
PATENT ASSIGNEE(S): Orquest, Inc., USA
SOURCE: U.S., 12 pp., Cont.-in-part of U. S. Ser. No.611,690, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5942499	A	19990824	US 1997-811971	19970305
CN 1212628	A	19990331	CN 1997-192822	19970305
NZ 331238	A	20000526	NZ 1997-331238	19970305
US 6645945	B1	20031111	US 1999-298539	19990422
US 6221854	B1	20010424	US 1999-360543	19990726
US 2001014664	A1	20010816	US 2001-825688	20010403
US 6703377	B2	20040309		
US 2004176295	A1	20040909	US 2004-796441	20040308
PRIORITY APPLN. INFO.:			US 1996-611690 B2	19960305
			US 1997-811971 A	19970305
			WO 1997-US4810 W	19970305
			US 1999-360543 A3	19990726
			US 2001-825688 A1	20010403

AB A bone growth-promoting composition is provided comprising hyaluronic acid and a growth factor. The composition has a viscosity and biodegradability sufficient to persist at the site of desired bone growth for a period of time sufficient to promote the bone growth. Preferably hyaluronic acid is used in a composition range of 0.1-4 % and preferred growth factor is bFGF, present in a concentration range of about 10-6 to 100 mg/mL.

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 34 OF 87 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:467044 CAPLUS
DOCUMENT NUMBER: 131:239377
TITLE: Fibulin-1 is a ligand for the C-type lectin domains of aggrecan and versican
AUTHOR(S): Aspberg, Anders; Adam, Susanne; Kostka, Gunter; Timpl, Rupert; Heinegard, Dick
CORPORATE SOURCE: Department of Cell and Molecular Biology, Section for Connective Tissue Biology, Lund University, Lund, SE-221 00, Swed.
SOURCE: Journal of Biological Chemistry (1999), 274(29), 20444-20449
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The aggregating proteoglycans (aggrecan, versican, neurocan, and brevican) are important components of many extracellular matrixes. Their N-terminal globular domain binds to hyaluronan, but the function of their C-terminal region containing a C-type lectin domain is less clear. We now report that a 90-kDa protein co-purifies with recombinant lectin domains from aggrecan and versican, but not from the brain-specific neurocan and brevican. Amino acid sequencing of tryptic peptides from this protein identified it as fibulin-1. This extracellular matrix glycoprotein is strongly expressed in tissues where versican is expressed (blood vessels, skin, and developing heart), and also expressed in developing cartilage and bone. It is thus likely to interact with these proteoglycans in vivo. Surface plasmon resonance measurements confirmed that aggrecan and versican lectin domains bind fibulin-1, whereas brevican and neurocan do not. As expected for a C-type lectin, the interactions with fibulin-1 are Ca2+-dependent, with KD values in the low nanomolar range. Using various deletion mutants, the binding site for aggrecan and versican lectin domains was mapped to the epidermal growth factor-like repeats in domain II of fibulin-1. No difference in affinity was found for deglycosylated fibulin-1, indicating that the proteoglycan C-type lectin domains bind to the protein part of fibulin-1.

REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 35 OF 87 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:482152 CAPLUS
DOCUMENT NUMBER: 129:265387
TITLE: Hyaluronate derivatives-based matrixes for growth factor delivery and tissue regeneration
AUTHOR(S): Liu, L. -S.; Thompson, A. Y.; Poser, J. W.; Spiro, R. C.
CORPORATE SOURCE: Orquest, Inc., Mountain View, CA, 94043, USA
SOURCE: Proceedings of the International Symposium on Controlled Release of Bioactive Materials (1998), 25th, 996-997
CODEN: PCRMEY; ISSN: 1022-0178
PUBLISHER: Controlled Release Society, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Two hyaluronate derivative-based matrixes, one an injectable gel and another an implantable sponge, were prepared In vitro anal. demonstrated that these matrixes provide a sustained release of growth factors. The release profile of incorporated growth factor can be modified by altering the method of incorporation. In vivo studies showed that the injected gel form of the matrix containing basic fibroblast growth factor can stimulate intramembranous bone formation. The sponge form of the matrix loaded with BMP enhanced bone formation when implanted in critical-sized cranial defects.

L18 ANSWER 36 OF 87 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:394664 CAPLUS
DOCUMENT NUMBER: 127:120338
TITLE: Nitric oxide degradation of heparin and heparan sulfate
AUTHOR(S): Vilar, Rolando E.; Ghael, Dineshchandra; Li, Min; Bhagat, Devan D.; Arrigo, Lisa M.; Cowman, Mary K.; Dweck, Harry S.; Rosenfeld, Louis
CORPORATE SOURCE: Neonatal Res. Lab., Division of Neonatology-Perinatology, Department of Pediatrics, New York Medical College, Valhalla, NY, 10595, USA
SOURCE: Biochemical Journal (1997), 324(2), 473-479
CODEN: BIJOAK; ISSN: 0264-6021
PUBLISHER: Portland Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB NO is a bioactive free radical produced by NO synthase in various tissues including vascular endothelium. One of the degradation products of NO is HNO2, an agent known to degrade heparin and heparan sulfate. This report documents degradation of heparin by cultured endothelial-cell-derived as well as exogenous NO. An exogenous narrow mol.-mass preparation of heparin was recovered from the medium of cultured endothelial cells using strong-anion exchange. In addition, another narrow mol.-mass preparation of heparin was gassed with exogenous NO under argon. Degradation was evaluated by gel-filtration chromatog. Since HNO2 degrades heparin under acidic conditions, the reaction with NO gas was studied under various pH conditions. Thus, the degradation of exogenous heparin by endothelial cells is inhibited by NO synthase inhibitors. Exogenous NO gas at concentration as low as 400 ppm degrades heparin and heparan sulfate. Exogenous NO degrades heparin at neutral as well as acidic pH. Endothelial-cell-derived NO, as well as exogenous NO gas, did not degrade hyaluronan, an unrelated glycosaminoglycan that resists HNO2 degradation Peroxynitrite, a metabolic product of the reaction of NO with superoxide, is an agent that degrades hyaluronan; however, peroxynitrite did not degrade heparin. Thus, endothelial-cell-derived NO is capable of degrading heparin and heparin sulfate via HNO2 rather than peroxynitrite. These observations may be relevant to various pathophysiol. processes in which extracellular matrix is degraded, such as bone development, apoptosis, tissue damage from inflammatory responses and possible release of growth factors and cytokines.
REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 37 OF 87 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:30677 CAPLUS
DOCUMENT NUMBER: 126:72882
TITLE: Bone matrix proteoglycans and glycoproteins
AUTHOR(S): Robey, Pamela Gehron
CORPORATE SOURCE: National Institute Dental Research, National Institutes Health, Bethesda, MD, 20892, USA
SOURCE: Principles of Bone Biology (1996), 155-165.
Editor(s): Bilezikian, John P.; Raisz, Lawrence G.; Rodan, Gideon A. Academic: San Diego, Calif.
CODEN: 63VKAS
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB A review with 46 refs. Bone matrix proteoglycans and glycoproteins are proportionally the most abundant constituents of the noncollagenous proteins in the bone matrix. Proteoglycans with protein cores composed of the leucine-rich repeat sequence (decorin, biglycan, fibromodulin, osteoadherin) are the predominant form found in mineralized matrix, although hyaluronan-binding forms (in

particular, versican), are present during early stages of osteogenesis. They participate in matrix formation and regulating growth factor activity. Glycoproteins such as alkaline phosphatase, osteonectin, and RGD-containing proteins (osteoadherin, thrombospondin, fibronectin, vitronectin, osteopontin, bone sialoprotein), fibrillin and tetranectin are produced at different stages of osteoblastic maturation. They exhibit a broad array of functions including control of cell proliferation, cell-matrix interactions, and mediation of hydroxyapatite deposition.

L18 ANSWER 38 OF 87 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:23931 CAPLUS
DOCUMENT NUMBER: 126:73106
TITLE: BMEC-1: A human bone marrow microvascular endothelial cell line with primary cell characteristics
AUTHOR(S): Candal, Francisco J.; Rafii, Shahin; Parker, Jeffery T.; Ades, Edwin W.; Ferris, Barbara; Nachman, Ralph L.; Kellar, Kathryn L.
CORPORATE SOURCE: Centers Disease Control and Prevention, National Center Infectious Diseases, Atlanta, GA, 30333, USA
SOURCE: Microvascular Research (1996), 52(3), 221-234
CODEN: MIVRA6; ISSN: 0026-2862
PUBLISHER: Academic
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Bone marrow microvascular endothelial cells (BMEC) are a functional component of the bone marrow stroma and have been shown to release hematopoietic regulatory factors as well as to selectively adhere and support the proliferation and differentiation of CD34+ hematopoietic progenitors. An early passage of these cells was immortalized by transfection with a vector (pSVT) encoding the large T antigen of SV40. The transformed cell line (CDC/CU.BMEC-1) expresses the SV40 transcript, retains the primary cell expression of Ulex europeaus and vWF/FVIII, and incorporates acetylated low-d. lipoprotein. In addition, BMEC-1 mirrors the phenotype of the primary cells with only a few exceptions. Both cell populations express the cellular adhesion mols. ICAM-1 and PECAM and also VCAM-1 and ELAM-1 after upregulation by tumor necrosis factor-α. The fibronectin receptor, hyaluronate receptor, collagen receptor, integrins VLA-α3, VLA-α4, and β4, endoglin, collagen IV, CD58, and CD61 are also expressed. The only differences are that BMEC-1 expresses higher levels of ICAM-1, CD58, CD34, CD36, and c-kit than the primary cells. The supernatants of primary cell and BMEC-1 contain stem cell factor, interleukin-6 (IL-6), granulocyte-macrophage colony-stimulating factor (GM-CSF), IL-1α, IL-11, and G-CSF. The functional significance of these hematopoietic cytokines was demonstrated in transwell cultures. Both cell populations supported the expansion of progeny from CD34+ cell-enriched cord blood mononuclear cells suspended in the upper chamber. These characteristics, plus the fact that BMEC-1 can be maintained independently of exogenous growth factors and exhibit contact inhibition, indicate that this cell line can be used to further define the role of BMEC in hematopoiesis.

L18 ANSWER 39 OF 87 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:392528 CAPLUS
DOCUMENT NUMBER: 125:77335
TITLE: Exogenous glycosaminoglycans (GAG) differentially modulate GAG synthesis by anchorage-independent cultures of the outer cells from neonatal rat calvaria in the absence and presence of TGF-β
AUTHOR(S): Anastassiades, Tassos P.; Chopra, Ravi K.; Wood, Anne
CORPORATE SOURCE: Dep. Medicine and Biochem., Queen's Univ., Kingston, ON, K7L 3N6, Can.
SOURCE: Molecular and Cellular Biochemistry (1996), 158(1),

25-32
CODEN: MCBIB8; ISSN: 0300-8177
PUBLISHER: Kluwer
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In anchorage-dependent (AD) cultures of the outer cell population (OCP) from neonatal rat calvaria, transforming growth factor -β1 (TGF-β) specifically upregulated the synthesis of chondroitin sulfate (CS) proteoglycan (PG) and uncoupled the inhibitory effect of increasing cell d. on CS PG synthesis. Utilizing the same cell population, we have further examined the possibility that glycosaminoglycan (GAG) known to be synthesized and secreted by bone cells might exert feedback effects on GAG synthesis and/or its stimulation by TGF-β. Although addition of TGF-β alone stimulated net synthesis of hyaluronic acid (HA) and CS in both AD and anchorage-independent (AI) cultures, significant alterations of basal and TGF-β-stimulated GAG synthesis by exogenous GAGs were observed only in AI cultures. In AI cultures exogenously added HA markedly enhanced the basal synthesis of HA and CS while heparin (H) suppressed the basal synthesis of HA, CS as well as dermatan sulfate (DS). Also, the addition of HA markedly potentiated the stimulation by TGF-β of HA and CS synthesis as did heparan sulfate (HS) for CS and DS synthesis. H suppressed the stimulation of the synthesis of HA, CS and DS by TGF-β. Overall, our results indicate specific effects of individual GAGs on basal and TGF-β-stimulated GAG synthesis in OCP cultures. We suggest that some of the GAGs in the OCP microenvironment (which with the exception of HA are covalently linked to protein cores of secreted PGs), acting in concert with TGF-β, may serve as an amplification system for upregulating GAG synthesis in the rapidly growing neonatal calvarium.

L18 ANSWER 40 OF 87 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:271222 CAPLUS
DOCUMENT NUMBER: 122:53692
TITLE: Effect of cytokines on prolactin production by human decidual stromal cells in culture: studies using cells freed of bone marrow-derived contaminants
AUTHOR(S): Vicovac, Ljiljana M.; Starkey, Phyllis M.; Aplin, John D.
CORPORATE SOURCE: INEP, University of Belgrade, Zemun, 11080, Yugoslavia
SOURCE: Journal of Clinical Endocrinology and Metabolism (1994), 79(6), 1877-82
CODEN: JCEMAZ; ISSN: 0021-972X
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Human decidua contains resident decidual cells alongside a population of bone marrow-derived cells, among which macrophages and large granular lymphocytes are most abundant. The authors hypothesized that soluble effectors produced by bone marrow-derived cells may modulate the function of the decidual cells. To investigate this, a cell purification protocol was devised that involved digestion of first-trimester decidua with collagenase and hyaluronidase to produce a mixed stromal cell suspension from which the bone marrow-derived cells were removed using immunomagnetic beads coated with anti-CD45. The resulting stromal cells were maintained in culture in the presence of progesterone and were found to produce PRL. The effect of a panel of cytokines on PRL production was examined Tumor necrosis factors-α and -β had a dose-dependent inhibitory effect, and tumor necrosis factor receptors were identified on the cells. Interleukin 1α and 1β, platelet-derived growth factor, and transforming growth factor-β1 were also found to inhibit PRL production, and platelet-derived growth factor and transforming growth factor-β1 stimulated cell proliferation. These findings suggest an interaction between the immune

and endocrine systems in regulating the maternal environment of early pregnancy.

L18 ANSWER 41 OF 87 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:603033 CAPLUS
DOCUMENT NUMBER: 121:203033
TITLE: Monocyte adhesion in patients with bone marrow fibrosis is required for the production of fibrogenic cytokines. Potential role for interleukin-1 and TGF-β
AUTHOR(S): Rameshwar, Pranela; Denny, Thomas N.; Stein, Dana; Gascon, Pedro
CORPORATE SOURCE: New Jersey Medical School, UMDNJ, Newark, NJ, 07103, USA
SOURCE: Journal of Immunology (1994), 153(6), 2819-30
CODEN: JOIMA3; ISSN: 0022-1767
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Idiopathic myelofibrosis (IMF) is a hemol. disorder characterized by bone marrow (BM) fibrosis. The BM contains excessive deposits of extracellular matrix proteins and exhibits neovascularization. The fibrosis is hypothesized to be a reactive phenomenon secondary to a clonal myeloid disorder. Growth factors such as platelet-derived growth factor (PDGF), TGF-β, and epidermal growth factor have been postulated as potential agents involved in BM fibrosis. The authors studied the induction of two fibrogenic cytokines, IL-1 and TGF-β, in IMF monocytes. High levels of both cytokines were produced in unstimulated IMF monocytes, compared with background levels produced in normal controls. Most of the TGF-β produced by IMF monocytes was in its active form. The spontaneous induction of IL-1α, IL-1β, and TGF-β in IMF monocytes parallels an increase in their steady state mRNA. Although high levels of cytoplasmic IL-1α, IL-1β, and TGF-β protein were detected in monocytes that were not subjected to any form of adherence, the secretion of these cytokines required adhesion. High levels of fibronectin, hyaluronic acid, and collagen, all potential ligands for the CD44 adhesion mol., have been reported in the circulation of IMF patients. However, the Ab-binding capacity of CD44 in IMF monocytes was reduced by 50% when compared with normal controls. Thus, monocytes and adhesion mols. may play a role in the induction of fibrogenic cytokines. These parameters may be important to the pathophysiol. of BM fibrosis.

L18 ANSWER 42 OF 87 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:213456 CAPLUS
DOCUMENT NUMBER: 120:213456
TITLE: Differential effects of bone associated factors on newly synthesized anionic glycoconjugates by articular chondrocyte cultures from adult and immature bovines
AUTHOR(S): Howard, Sarah; Anastassiades, Tassos
CORPORATE SOURCE: Dep. Med., Queen's Univ., Kingston, ON, K7L 3N6, Can.
SOURCE: Journal of Rheumatology (1993), 20(12), 2083-94
CODEN: JRHUA9; ISSN: 0315-162X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors determined if bone-associated peptide factors (BAF) differentially affect proteoglycan and hyaluronic acid (HA) synthesis as a result of the maturity of the animal and of the location of chondrocytes within cartilage zones. Calf and adult bovine articular chondrocytes were isolated and cultured, as high-d. monolayers, with 3H-glucosamine and 35S-sulfate. The effects of com. transforming growth factor β (TGF-β) and a preparation from bovine bone that contained the total extractable stimulatory activity for glycosaminoglycan (GAG) synthesis (matrigenin activity) were

studied. Calf chondrocytes spontaneously synthesized a higher proportion of proteoglycans of larger hydrodynamic size, but the addition of the BAF resulted in a proportionally greater shift in the adult chondrocytes towards the synthesis of larger proteoglycans, appearing in the medium. Subpopulations of adult chondrocytes from the deep zone synthesized spontaneously more chondroitin sulfate (CS) and less HA than chondrocytes from the superficial zone, but the calf chondrocytes from the 3 zones showed similar patterns of GAG synthesis. Adult chondrocytes from the deep zone had large responses to the BAF for HA but not CS synthesis, resembling the subpopulations of the calf chondrocytes. BAF differentially modulate HA and CS synthesis of articular chondrocytes as a result of maturation and topog. The authors speculate as to how this differential response to BAF may help set the stage for the progression of osteoarthritis in weight-bearing joints.

L18 ANSWER 43 OF 87 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:74438 CAPLUS
DOCUMENT NUMBER: 120:74438
TITLE: Human acute myeloid leukemia cells bind to bone marrow stroma via a combination of β-1 and β-2 integrin mechanisms
AUTHOR(S): Bendall, Linda J.; Kortlepel, Kim; Gottlieb, David J.
CORPORATE SOURCE: Dep. Haematol., Westmead Hosp., Westmead, 2145, Australia
SOURCE: Blood (1993), 82(10), 3125-32
CODEN: BLOOAW; ISSN: 0006-4971
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Acute myeloid leukemia (AML) cells respond to exogenous stimulation from myeloid growth factors that may be secreted by cells of the bone marrow (BM) stroma and retained by glycosaminoglycans in the extracellular matrix. The authors have analyzed the capacity of malignant cells from patients with AML to maintain close proximity to sites of growth factor production and retention by binding to BM stromal elements, including fibroblasts and extracellular matrix proteins. Leukemic cells from all cases of AML adhered to BM fibroblast (BMF) monolayers (mean ± SE percentage binding, 30.9% ± 2.5%) and to fibronectin and laminin (mean ± SE percentage binding, 28.0% ± 4.1% and 21.5% ± 2.3%, resp.). Binding to bovine and human collagen type 1, vitronectin, hyaluronic acid, and albumin was minimal. Anal. of binding mechanisms indicated that very late antigen-4 (VLA-4) and VLA-5 were responsible for AML cell binding to fibronectin. Binding to laminin could be inhibited by antibody to the α chain of VLA-6. In contrast, AML cell adhesion to BMF monolayers was not impaired by blocking antibodies to either β1 or β1 integrins used alone, although the combination of anti-CD11/CD18 and anti-VLA-4 inhibited binding in more than 50% of cases. When anti-VLA-5 was added in these cases, mean ± SE inhibition of binding of 45.5% ± 9.1% was observed Binding of AML cells to extracellular matrix proteins fibronectin and laminin is predominantly β1-integrin-dependent, but AML cell adhesion to BMF relies on the simultaneous involvement of β1 and β2 integrins as well as other currently unrecognized ligands.

L18 ANSWER 44 OF 87 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:515218 CAPLUS
DOCUMENT NUMBER: 119:115218
TITLE: Hyaluronate activation of CD44 induces insulin-like growth factor-1 expression by a tumor necrosis factor-α-dependent mechanism in murine macrophages
AUTHOR(S): Noble, Paul W.; Lake, Fiona R.; Henson, Peter M.; Riches, David W. H.
CORPORATE SOURCE: Dep. Pediatr., Natl. Jew. Cent. Immunol. Respir. Med.,

Denver, CO, 80206, USA
SOURCE: Journal of Clinical Investigation (1993), 91(6), 2368-77
CODEN: JCINAO; ISSN: 0021-9738
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Macrophages participate in inflammatory and repair processes in part through the selective release of cytokines that contribute to tissue remodeling. Extracellular matrix components generated at inflammatory sites may influence tissue remodeling by effects on leukocyte adherence and local cytokine production In murine bone marrow-derived macrophages, it was found that soluble hyaluronic acid stimulated IL-1β, TNFα, and insulin-like growth factor -1 (IGF-1) mRNA transcript expression as well as IGF-1 protein synthesis. Monoclonal antibodies to the hyaluronic acid receptor CD44 blocked the effects of hyaluronic acid on IL-1β, TNFα, and IGF-1 expression. TNFα and IL-1β mRNA expression preceded IGF-1 protein synthesis, and TNFα, but not IL-1β, was found to directly stimulate IGF-1. Furthermore, IGF-1 induction was dependent on endogenous TNFα production since IGF-1 protein synthesis was inhibited in the presence of anti-TNFα antiserum. In addition, IL-1β was found to exert a regulatory role on IGF-1 production by enhancing the TNFα effect. IL-1β and TNFα mRNA transcript expression as well as IGF-1 protein synthesis were also stimulated by chrysotile asbestos. Anti-CD44 antibodies had no effect whereas anti-TNFα antiserum blocked asbestos-stimulated IGF-1 production Thus, hyaluronate activation of CD44 induces cytokine expression and macrophage-derived IGF-1 production is dependent on TNFα expression.

L18 ANSWER 45 OF 87 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:456097 CAPLUS
DOCUMENT NUMBER: 119:56097
TITLE: A collagen/DBP sponge system designed for in vitro analysis of chondroinduction
AUTHOR(S): Mizuno, Shuichi; Lycette, Chris; Quinto, Charlene; Glowacki, Julie
CORPORATE SOURCE: Brigham and Women's Hosp., Boston, MA, 02115, USA
SOURCE: Materials Research Society Symposium Proceedings (1992), 252(Tissue-Inducing Biomaterials), 133-40
CODEN: MRSPDH; ISSN: 0272-9172
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In response to s.c. implants of demineralized bone powder (DBP), cells are attracted to the DBP, are converted to chondroblasts, and produce a cartilage matrix that is resorbed and replaced by bone . To define the cellular mechanisms of this induction, a collagen sponge model was developed for simulating the in vivo environment and for promoting the ingrowth and viability of cells cultured in them in vitro. Reconstituted pepsin-digested type I collagen from bovine hide was neutralized. Rat DBP (75-250 μm) was added into the collagen mixture (20 mg/mL). In order to simulate the connective tissue environment, modified chondroitin sulfate, heparan sulfate, or hyaluronic acid was added into the mixture Human dermal fibroblasts were cultured from minced fresh tissue and inoculated at 1.5 + 105 cells/sponge. Fifteen hours later, some sponges were transferred to medium which contained growth factors (PDGF or TGF-β). The inoculated cells attached to the collagen fibers and migrated into the sponge. Eventually the sponges contracted and acquired an oval shape. Cells on or near DBP were ovoid or stellate in shape. Cell morphol. was modulated by glycosaminoglycan composition of the sponge. Increasing doses of PDGF or TGF-β promoted cellularity within the sponges. This system simulates the in vivo environment but allows accessibility for anal. This 3-dimensional matrix culture system will enable investigation of

mechanisms of chondroinduction by morphogenic material.

L18 ANSWER 46 OF 87 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1991:178974 CAPLUS
DOCUMENT NUMBER: 114:178974
TITLE: Newly synthesized proteoglycans secreted by sequentially derived populations of cells from new-born rat calvaria: Effects of transforming growth factor-β and matrigenin activity
AUTHOR(S): Chopra, Ravi K.; Li, Zhen Min; Vickery, Sylvia; Anastassiades, Tassos
CORPORATE SOURCE: Dep. Med., Queen's Univ., Kingston, ON, K7L 3N6, Can.
SOURCE: Cell Differentiation and Development (1990), 32(1), 47-59
CODEN: CDDEE8; ISSN: 0922-3371
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Three populations (1, 3, and 6) of bone cells, derived from rat calvaria by sequential enzymic digestion, were cultured with [3H]glucosamine and [35S]sulfate, in the presence or absence of transforming growth factor-β (TGF-β) or bone-derived matrigenin activity. Population 6 synthesized a chondroitin sulfate proteoglycan (PG) and responded to the addition of the factors by increased rates of synthesis of hyaluronic acid (HA) and PG and an increase in the size in the size of HA. Comparisons of populations 1, 3, and 6 showed an ordered, spontaneous increase in HA and PG synthesis. However, the addition of matrigenin activity resulted in a much greater stimulation of PG, but not HA, synthesis in population 1 compared to population 6, suggesting a cellular organization in the calvarium whose net effect would be to direct PG synthesis towards the periphery of the tissue.

L18 ANSWER 1 OF 87 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:365040 CAPLUS
DOCUMENT NUMBER: 144:419681
TITLE: Platelet-derived growth factor compositions and methods of use thereof
INVENTOR(S): Lynch, Samuel E.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 22 pp., Cont.-in-part of U.S. Ser. No. 965,319, abandoned.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006084602	A1	20060420	US 2005-159533	20050623
WO 2006044334	A2	20060427	WO 2005-US36447	20051012

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2004-965319 B2 20041014
US 2005-159533 A1 20050623

AB A method for promoting growth of bone, periodontium, ligament, or cartilage in a mammal by applying to the bone, periodontium, ligament, or cartilage a composition comprising platelet-derived growth factor at a concentration in the range of about 0.1 mg/mL to about 1.0 mg/mL in a pharmaceutically acceptable liquid carrier and a pharmaceutically-acceptable solid carrier.

L18 ANSWER 2 OF 87 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:343183 CAPLUS
DOCUMENT NUMBER: 144:376579
TITLE: Hyaluronic acid-coated bone implant device
INVENTOR(S): Gazza, Gianluca
PATENT ASSIGNEE(S): Bayco Consulting Limited, UK
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006038056	A1	20060413	WO 2004-IB3260	20041006

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,

IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: WO 2004-IB3260 20041006

AB The present invention relates to a bone implant device, particularly for dental and orthopedic prosthesis on the vertebral column, having a quicker osteo-integration compared to the prior art devices. Particularly, the present invention relates to an implant device, of metal or polymer nature, a layer of hyaluronic acid being chemical bound on the surface thereof, for use in applications in contact with the bone, with activity of stimulating the bone tissue growth, as well as a process for preparing the same. For example, titanium samples (1 cm2 squares) were subjected to a plasma deposition of allylamine, followed by immersion in a pretreated hyaluronic acid solution (0.5%). The considerable reduction of cell adhesion to hyaluronic acid-modified titanium surface was observed, compared to non-modified titanium surface.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 3 OF 87 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1293771 CAPLUS

DOCUMENT NUMBER: 144:27688

TITLE: Bone tissue engineering by ex vivo stem cells ongrowth into three-dimensional trabecular metal

INVENTOR(S): Xuenong, Zou; Li, Haisheng; Bunger, Cody

PATENT ASSIGNEE(S): Den.

SOURCE: U.S. Pat. Appl. Publ., 10 pp.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005272153	A1	20051208	US 2005-45620	20050127

PRIORITY APPLN. INFO.: US 2004-539661P P 20040127

AB Adult autologous stem cells cultured on a porous, three-dimensional tissue scaffold-implant for bone regeneration by the use of a hyaluronan and/or dexamethasone to accelerate bone healing alone or in combination with recombinant growth factors or transfected osteogenic genes. The scaffold-implant may be machined into a custom-shaped three-dimensional cell culture system for support of cell growth, reservoir for peptides, recombinant growth factors, cytokines and antineoplastic drugs in the presence of a hyaluronan and/or dexamethasone alone or in combination with growth factors or transfected osteogenic genes, to be assembled ex vivo in a tissue incubator for implantation into bone tissue.

L18 ANSWER 4 OF 87 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1242488 CAPLUS

DOCUMENT NUMBER: 143:483255

TITLE: Cartilage repair mixture containing allograft chondrocytes and a polymeric carrier

INVENTOR(S): Truncale, Katherine Ann Gomes; Gertzman, Arthur A.

PATENT ASSIGNEE(S): Musculoskeletal Transplant Foundation, USA

SOURCE: PCT Int. Appl., 15 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005110278	A2	20051124	WO 2005-US8798	20050316

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2004-566618P P 20040430

AB The invention is directed toward a sterile cartilage defect implant material comprising milled lyophilized allograft cartilage pieces ranging from 0.01 mm to 1.0 mm in size in a bioabsorbable carrier taken from a group consisting of sodium hyaluronic acid and its derivs., gelatin, collagen, chitosan, alginate, buffered PBS, dextran or mixed polymers with allograft chondrocytes added in an amount ranging from 2.5 x 105 to 2.5 x 107. A cartilage repair implant material further includes an additive consisting of one or more of a group consisting of growth factors, human allogenic cells, human allogenic and autologous bone marrow cells, human allogenic and autologous stem cells, demineralized bone matrix, and insulin.

L18 ANSWER 5 OF 87 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:493531 CAPLUS

DOCUMENT NUMBER: 143:48168

TITLE: Composite structures containing hyaluronic acid the derivatives thereof as new bone substitutes and grafts

INVENTOR(S): Pastorello, Andrea; Pressato, Daniele

PATENT ASSIGNEE(S): Fidia Advanced Biopolymers S.r.L., Italy

SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005051446	A1	20050609	WO 2004-EP53129	20041126

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: IT 2003-PD286 A 20031127

AB A composite material comprises: (i) hyaluronic acid and/or hyaluronic acid derivs., (ii) demineralized bone and/or biocompatible partially or totally demineralized bone tissue matrix and/or biocompatible and bioresorbable ceramic materials. This material preferably associated with at least one layer comprising a hyaluronic acid derivative may be used in the preparation of bone substitutes or grafts for the regeneration or formation of bone

tissue in surgery. Preparation of a composite matrixes of hydroxyapatite and/or of bone structures, containing/incorporating crosslinked hyaluronic acid.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 6 OF 87 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:328081 CAPLUS
DOCUMENT NUMBER: 142:451774
TITLE: Absorbable ultrafine fiber tissue repair material and its preparation
INVENTOR(S): Li, Xinsong
PATENT ASSIGNEE(S): Dongnan University, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 10 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1456360	A	20031119	CN 2003-131587	20030528
PRIORITY APPLN. INFO.:			CN 2003-131587	20030528

AB The tissue repair material is prepared from Ca phosphate ultrafine particle and absorbable ultrafine polymer fiber (at a ratio of 1-2:1-9) and/or 5% bioactive substance. The Ca phosphate ultrafine particle with size <5 μm is hydroxyapatite, Ca3(PO4)2, Ca2P2O7, CaHPO4, and/or CaHPO4 2H2O. The absorbable ultrafine polymer fiber is polylactic acid, polyglycolic acid, polycaprolactone, polybutyrolactone, polypentanolactone, polyanhydride, poly-alpha-amino acid, their copolymer, chitosan, hyaluronic acid, chondroitin sulfate, collagen, carrageenan, alginate, gelatin, glucan, fibroin, keratin, albumin, and/or their derivative The bioactive substance is bone morphogenetic protein, gliacyte growth factor, transforming growth factor, insulin-like growth factor, platelet derived growth factor, fibroblast growth factor, antibiotics, immunosuppressant, antibacterial agent, hormone, vitamin, amino acid, peptide, protein, and/or enzyme.

L18 ANSWER 7 OF 87 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:947683 CAPLUS
DOCUMENT NUMBER: 142:149037
TITLE: Synergistic roles of BMP15 and GDF9 in the development and function of the oocyte-cumulus cell complex in mice: genetic evidence for an oocyte-granulosa cell regulatory loop
AUTHOR(S): Su, You-Qiang; Wu, Xuemei; O'Brien, Marilyn J.; Pendola, Frank L.; Denegre, James N.; Matzuk, Martin M.; Eppig, John J.
CORPORATE SOURCE: The Jackson Laboratory, Bar Harbor, ME, 04609, USA
SOURCE: Developmental Biology (San Diego, CA, United States) (2004), 276(1), 64-73
CODEN: DEBIAO; ISSN: 0012-1606
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Bone morphogenetic protein 15 (BMP15) and growth differentiation factor 9 (GDF9) are oocyte-specific growth factors that appear to play key roles in granulosa cell development and fertility in most mammalian species. We have evaluated the role(s) of these paracrine factors in the development and function of both the cumulus cells and oocytes by assessing cumulus expansion, oocyte maturation, fertilization, and preimplantation embryogenesis in Gdf9+/-Bmp15-/-

[hereafter, double mutant (DM)] mice. We found that cumulus expansion, as well as the expression of hyaluronan synthase 2 (Has2) mRNA was impaired in DM oocyte-cumulus cell complexes. This aberrant cumulus expansion was not remedied by coculture with normal wild-type (WT) oocytes, indicating that the development and/or differentiation of cumulus cells in the DM, up to the stage of the preovulatory LH surge, is impaired. In addition, DM oocytes failed to enable FSH to induce cumulus expansion in WT oocytectomized (OOX) cumulus. Moreover, LH-induced oocyte meiotic resumption was significantly delayed in vivo, and this delayed resumption of meiosis was correlated with the reduced activation of mitogen-activated protein kinase (MAPK) in the cumulus cells, thus suggesting that GDF9 and BMP15 also regulate the function of cumulus cells after the preovulatory LH surge. Although spontaneous in vitro oocyte maturation occurred normally, oocyte fertilization and preimplantation embryogenesis were significantly altered in the DM, suggesting that the full complement of both GDF9 and BMP15 are essential for the development and function of oocytes. Because receptors for GDF9 and BMP15 have not yet been identified in mouse oocytes, the effects of the mutations in the Bmp15 and Gdf9 genes on oocyte development and functions must be produced indirectly by first affecting the granulosa cells and then the oocyte. Therefore, this study provides further evidence for the existence and functioning of an oocyte-granulosa cell regulatory loop.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 8 OF 87 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:595461 CAPLUS
DOCUMENT NUMBER: 141:337817
TITLE: Sclerous tissue repairing material and its preparing method
INVENTOR(S): Li, Xinsong; Pu, Yuepu; Ye, Lang
PATENT ASSIGNEE(S): Dongnan University, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 9 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1403167	A	20030319	CN 2002-138344	20020926

PRIORITY APPLN. INFO.: CN 2002-138344 20020926

AB The sclerous tissue repairing material is composed of <100 μm Ca phosphate (such as Ca10(PO4)6(OH)2, Ca3(PO4)2, Ca2P2O7, CaHPO4, and/or CaHPO4 2H2O) 5-80, biol. absorbable high polymer 10-85, demineralized bone <1-70, and additive <5%. The biol. absorbable high polymer is polylactic acid, polyglycolic acid, polycaprolactone, polybutyrolactone, polyvalerolactone, polyanhydride, poly-alpha-amino acid, copolymer of lactic acid (glycolic acid, caprolactone, butyrolactone, valerolactone, and/or amino acid), chitin or its derivative, chitosan or its derivative, hyaluronic acid or its derivative, collagen, carrageenan, Na alginate, Ca alginate, chondroitin sulfate, gelatin, agar, glucosan, fiber protein, silk protein, keratoprotein, casein, albumin, elastin, flock, filament, yarn, non-woven fabric, etc. The additive is human bone morphogenetic protein (BMP), BMP-1, BMP-2, BMP-3, BMP-4, BMP-5, BMP-6, BMP-7, BMP-8, growth/differentiation factor GDF-5, GDF-6, GDF-7, transforming growth factor beta, insulin-like growth factor, platelet-derived growth factor, osteoblast growth factor, antibiotic, immunosuppressant, antibacterial agent, hormone, vitamin, amino acid, peptide, protein, and/or enzyme.

L18 ANSWER 9 OF 87 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:595460 CAPLUS
DOCUMENT NUMBER: 141:337816
TITLE: Absorbable active composition for repairing sclerous tissue and its preparing method
INVENTOR(S): Li, Xinsong; Pu, Yuepu; Ha, Yongquan; Zou, Jun; Zhang, Guoqing
PATENT ASSIGNEE(S): Dongnan University, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 11 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1403166	A	20030319	CN 2002-138343	20020926

PRIORITY APPLN. INFO.: CN 2002-138343 20020926

AB The absorbable active composition is composed of <100 μm Ca phosphate (such as Ca10(PO4)6(OH)2, Ca3(PO4)2, Ca2P2O7, CaHPO4, and/or CaHPO4 2H2O) 5-80, biol. absorbable high polymer 10-90, bone growth factor <10, and additive <4%. The biol. absorbable high polymer is polylactic acid, polyglycolic acid, polycaprolactone, polybutyrolactone, polyvalerolactone, polyanhydride, poly-alpha-amino acid, copolymer of lactic acid (glycolic acid, caprolactone, butyrolactone, valerolactone, and/or amino acid), chitin or its derivative, chitosan or its derivative, hyaluronic acid or its derivative, collagen, carrageenan, Na alginate, Ca alginate, chondroitin sulfate, gelatin, agar, glucosan, fiber protein, silk protein, keratoprotein, casein, albumin, elastin, flock, filament, yarn, non-woven fabric, etc. The bone growth factor is human bone morphogenetic protein, BMP-1, BMP-2, BMP-3, BMP-4, BMP-5, BMP-6, BMP-7, BMP-8, growth/differentiation factor GDF-5, GDF-6, GDF-7, transforming growth factor beta, insulin-like growth factor, platelet-derived growth factor, and/or osteoblast growth factor. The additive is antibiotic, immunosuppressant, antibacterial agent, hormone, vitamin, amino acid, peptide, protein, and/or enzyme.

L18 ANSWER 10 OF 87 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:595459 CAPLUS
DOCUMENT NUMBER: 141:337815
TITLE: Active composition for repairing sclerous tissues and its preparing method
INVENTOR(S): Li, Xinsong; Pu, Yuepu; Ye, Lang
PATENT ASSIGNEE(S): Dongnan University, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 9 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1403165	A	20030319	CN 2002-138342	20020926

PRIORITY APPLN. INFO.: CN 2002-138342 20020926

AB The active composition is composed of <100 μm Ca phosphate6(OH)2, Ca3(PO4)2, Ca2P2O7, CaHPO4, and/or CaHPO4 2H2O 8-80, biol. absorbable high polymer 10-85, active substance <50, and additive <5%. The biol. absorbable high polymer is polylactic acid, polyglycolic acid, polycaprolactone, polybutyrolactone, polyvalerolactone, polyanhydride, poly-alpha-amino acid, copolymer of lactic acid (glycolic acid, caprolactone, butyrolactone, valerolactone, and/or amino acid), chitin or its derivative,

chitosan or its derivative, hyaluronic acid or its derivative, collagen, carrageenan, Na alginate, Ca alginate, chondroitin sulfate, gelatin, agar, glucosan, fiber protein, silk protein, keratoprotein, casein, albumin, elastin, flock, filament, yarn, non-woven fabric, etc. The active substance is bone marrow, marrow cell, stem cell, osteoblast, or chondrocyte. The additive is human bone morphogenetic protein (BMP), BMP-1, BMP-2, BMP-3, BMP-4, BMP-5, BMP-6, BMP-7, BMP-8, growth/differentiation factor GDF-5, GDF-6, GDF-7, transforming growth factor beta, insulin-like growth factor, platelet-derived growth factor, osteoblast growth factor, antibiotic, immunosuppressant, antibacterial agent, hormone, vitamin, amino acid, peptide, protein, and/or enzyme.

L18 ANSWER 11 OF 87 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:411200 CAPLUS
DOCUMENT NUMBER: 141:86611
TITLE: Control of angiogenesis by inhibitor of phospholipase A2
AUTHOR(S): Chen, Wenming; Li, Lihong; Zhu, Jiazhi; Liu, Jinwei; Soria, Jeannette; Soria, Claudine; Yedgar, Saul
CORPORATE SOURCE: Beijing Chaoyang Hospital, Capital University of Medical Sciences, Beijing, 100020, Peop. Rep. China
SOURCE: Chinese Medical Sciences Journal (2004), 19(1), 6-12
CODEN: CMSJEP; ISSN: 1001-9294
PUBLISHER: Chinese Academy of Medical Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Objective To investigate the potential effects of angiogenic process by secretory phospholipase A2 (sPLA2) inhibitor-HyPE (linking N-derivatized phosphatidyl-ethanolamine to hyaluronic acid) on human bone marrow endothelial cell line (HBME-1). Methods In order to examine the suppressing effects of HyPE on HBME-1 proliferation, migration, and capillary-like tube formation, HBME-1 were activated by angiogenic factor, specifically by basic fibroblast growth factor (b-FGF), vascular endothelial growth factor (VEGF), and oncostatin M (OSM) (at a final concentration of 25, 20, and 2.5 ng/mL, resp.), then HBME-1 proliferation, migration, and tube formation were studied in the absence or presence of HyPE. HBME-1 tube formation was specially analyzed in fibrin gel. Results HyPE effectively inhibited HBME-1 proliferation and migration as a dose-dependent manner, whatever HBME-1 were grown in the control culture medium or stimulated with b-FGF, VEGF, or OSM. In fibrin, the formations of HBME-1 derived tube-like structures were enhanced by all angiogenic factors, but these were strongly suppressed by HyPE. Conclusions The results support the involvement of sPLA2 in angiogenesis. It is proposed that sPLA2 inhibitor introduces a novel approach in the control of cancer development.
REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 12 OF 87 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:353355 CAPLUS
DOCUMENT NUMBER: 141:86967
TITLE: Gene expression profiling in glomeruli from human kidneys with diabetic nephropathy
AUTHOR(S): Baelde, Hans J.; Eikmans, Michael; Doran, Peter P.; Lappin, David W. P.; De Heer, Emile; Bruijn, Jan A.
CORPORATE SOURCE: Department of Pathology, Leiden University Medical Center, Leiden, Neth.
SOURCE: American Journal of Kidney Diseases (2004), 43(4), 636-650
CODEN: AJKDDP; ISSN: 0272-6386
PUBLISHER: W. B. Saunders Co.
DOCUMENT TYPE: Journal

LANGUAGE: English

AB Diabetic nephropathy (DN) is a frequent complication in patients with diabetes mellitus. To find improved intervention strategies in this disease, it is necessary to investigate the mol. mechanisms involved. To obtain more insight into processes that lead to DN, mRNA expression profiles of diabetic glomeruli and glomeruli from healthy individuals were compared. Two morphol. normal kidneys and 2 kidneys from patients with DN were used for the study. Glomerular RNA was hybridized in duplicate on Human Genome U95Av2 Arrays (Affymetrix, Santa Clara, CA). Several transcripts were tested further in independent patient groups and at the protein level by immunohistochem. Ninety-six genes were upregulated in diabetic glomeruli, whereas 519 genes were downregulated. The list of overexpressed genes in DN includes aquaporin 1, calpain 3, hyaluronoglucosidase, and platelet/endothelial cell adhesion mol. The list of downregulated genes includes bone morphogenetic protein 2, vascular endothelial growth factor (VEGF), fibroblast growth factor 1, insulin-like growth factor binding protein 2, and nephrin. A decrease in VEGF and nephrin could be validated at the protein level and also at the RNA level in renal biopsy specimens from 5 addnl. patients with diabetes. Results of oligonucleotide microarray analyses on control and diabetic glomeruli are presented and discussed in their relation to vascular damage, mesangial matrix expansion, proliferation, and proteinuria. The findings suggest that progression of DN might result from diminished tissue repair capability.

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 13 OF 87 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:142901 CAPLUS

DOCUMENT NUMBER: 140:169759

TITLE: Method of applying hyaluronic acid to implant or graft to enhance lubricity and cellular density

INVENTOR(S): Grafton, R. Donald

PATENT ASSIGNEE(S): Arthrex, Inc., USA

SOURCE: PCT Int. Appl., 13 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004014303	A2	20040219	WO 2003-US24639		20030808
WO 2004014303	A3	20060608			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
US 2004180822	A1	20040916	US 2003-635444		20030807
AU 2003257208	A1	20040225	AU 2003-257208		20030808
PRIORITY APPLN. INFO.:			US 2002-402068P	P	20020809
			WO 2003-US24639	W	20030808

AB A method for lubricating an implant or graft prior to implantation into a target implant site which enhances the lubricity of the implant or graft and promotes bone growth. The method comprises the steps of lubricating the implant or graft with the composition comprising

hyaluronic acid and optionally a growth factor and/or an antiseptic and/or antibiotic, and subsequently implanting the lubricated implant or graft into a target implant site.

L18 ANSWER 14 OF 87 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:882869 CAPLUS
DOCUMENT NUMBER: 139:369785
TITLE: Calcium phosphate-based bone fillers and their manufacture
INVENTOR(S): Inoe, Akira; Yauchi, Takeshi; Hibino, Hiroki; Saito, Ryoji
PATENT ASSIGNEE(S): Olympus Optical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 7 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2003320009	A2	20031111	JP 2002-129264	20020430
PRIORITY APPLN. INFO.:			JP 2002-129264	20020430

AB Mesenchymal stem cell-containing concs. obtained by removal of unnecessary components from the body fluid are added to bone fillers comprising β-Ca3(PO4)2. Preferably, the bone fillers may also contain concentrated blood platelets, fibrin, growth factors selected from bone morphogenetic protein, FGF, TGF-β, IGF, PDGF, VEGF, and HGF, and bioabsorbable organic materials selected from fibrin, poly(lactic acid), poly(glycolic acid), lactic acid-glycolic acid copolymer, collagen, gelatin, chitin-chitosan, hyaluronic acid, alginic acid, and their modification products. The bone fillers increase the rates of repair of bone defects after surgery.

L18 ANSWER 15 OF 87 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:783826 CAPLUS
DOCUMENT NUMBER: 140:264409
TITLE: Hyaluronic acid reverses the abnormal synthetic activity of human osteoarthritic subchondral bone osteoblasts
AUTHOR(S): Lajeunesse, Daniel; Delalandre, Aline; Martel-Pelletier, Johanne; Pelletier, Jean-Pierre
CORPORATE SOURCE: Unite de recherche en Arthrose, Centre de recherche du Centre Hospitalier de I'Universite de Montreal, Montreal, QC, H2L 4M1, Can.
SOURCE: Bone (San Diego, CA, United States) (2003), 33(4), 703-710
CODEN: BONEDL; ISSN: 8756-3282
PUBLISHER: Elsevier Science
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The underlying mechanisms responsible for both cartilage loss and subchondral bone changes in osteoarthritis (OA) remain unknown. It is becoming recognized that the extracellular matrix influences the metabolism of cells both in vivo and in vitro and can modify their responses to external stimuli. Indeed, the glycosaminoglycan/proteoglycan matrix is of major importance for the proliferation and/or differentiation of a number of cells. Here, we determined the potential role of hyaluronic acid (HA) of increasing mol. weight (MW) to alter the expression of metabolic markers and cytokine production by human osteoarthritic (OA) subchondral osteoblasts (Ob). Both 1,25(OH)2D3-induced alkaline phosphatase activity (ALPase) and osteocalcin release were increased in OA Ob when compared to normal. HA reduced osteocalcin release in OA Ob at MW of 300 and above,

whereas HA failed to significantly modify ALPase. Parathyroid hormone (PTH) stimulated cAMP (cAMP) formation by OA Ob. HA had a biphasic effect on this PTH-dependent activity, totally inhibiting cAMP formation at MW of 300 and 800. HA of increasing MW progressively reduced the levels of Prostaglandin E2 (PGE2) and interleukin-6 (IL-6) produced by OA Ob. Interestingly, urokinase plasminogen activator (uPA) and PA inhibitor-1 (PAI-1) levels were not significantly affected by HA of increasing MW; however, the PAI-1 to uPA ratio showed a slight, yet nonsignificant increase. Surprisingly, uPA activity was increased in OA Ob under the same conditions. Last, HA had no effect on the production of insulin-like growth factor-1 by these cells. Our data suggest that high MW HA can modify cellular parameters in OA Ob that are increased when compared to normal. The effect of HA on inflammatory mediators, such as PGE2 and IL-6, and on uPA activity is more striking at higher MW as well. Taken together, these results could suggest that HA of increasing MW has pos. effects on OA Ob by modifying their biol. synthetic capacities.

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 16 OF 87 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:594556 CAPLUS

DOCUMENT NUMBER: 139:148255

TITLE: The role of autocrine FGF-2 in the distinctive bone marrow fibrosis of hairy-cell leukemia (HCL)

AUTHOR(S): Aziz, Khalil A.; Till, Kathleen J.; Chen, Haijuan; Slupsky, Joseph R.; Campbell, Fiona; Cawley, John C.; Zuzel, Mirko

CORPORATE SOURCE: Department of Haematology, University of Liverpool, UK

SOURCE: Blood (2003), 102(3), 1051-1056
CODEN: BLOOAW; ISSN: 0006-4971

PUBLISHER: American Society of Hematology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Bone marrow (BM) fibrosis is a central diagnostic and pathogenetic feature of hairy-cell leukemia (HCL). It is known that fibronectin (FN) produced and assembled by the malignant hairy cells (HCs) themselves is a major component of this fibrosis. It is also known that FN production is greatly enhanced by adhesion of HCs to hyaluronan (HA) via CD44. The aim of the present study was to establish the roles of fibrogenic autocrine cytokines (fibroblast growth factor -2 [FGF-2] and transforming growth factor β [TGFβ]) and of different isoforms of CD44 in this FN production We show that HC adhesion to HA stimulates FGF-2, but not TGFβ, production and that HCs possess FGF-2 receptor. In a range of expts., FN production was greatly reduced by blocking FGF-2 but not TGFβ. Moreover FN, but not FGF-2, secretion was blocked by down-regulation of the v3 isoform of CD44 and by addition of heparitinase. These results show that autocrine FGF-2 secreted by HCs is the principal cytokine responsible for FN production by these cells when cultured on HA. The central role of FGF-2 in the pathogenesis of the BM fibrosis of HCL was supported by our immunohistochem. demonstration of large amts. of this cytokine in fibrotic BM but not in HCL spleen where there is no fibrosis. As regards CD44 isoforms, the present work demonstrates that CD44v3 is essential for providing the heparan sulfate necessary for HC stimulation by FGF-2, whereas the signal for production of the cytokine was provided by HA binding to CD44H, the standard hematopoietic form of the mol.

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 17 OF 87 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:459340 CAPLUS

DOCUMENT NUMBER: 140:71085

TITLE: Local roles of TGF-β superfamily members in the control of ovarian follicle development

AUTHOR(S): Knight, Philip G.; Glister, Claire
CORPORATE SOURCE: School of Animal and Microbial Sciences, University of Reading, Whiteknights, Reading, RG6 6AJ, UK
SOURCE: Animal Reproduction Science (2003), 78(3,4), 165-183
CODEN: ANRSDV; ISSN: 0378-4320
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Members of the transforming growth factor -β (TGF-β) superfamily have wide-ranging influences on many tissue and organ systems including the ovary. Two recently discovered TGF-β superfamily members, growth/differentiation factor-9 (GDF-9) and bone morphogenetic protein-15 (BMP-15; also designated as GDF-9B) are expressed in an oocyte-specific manner from a very early stage and play a key role in promoting follicle growth beyond the primary stage. Follicle growth to the small antral stage does not require gonadotrophins but appears to be driven by local autocrine/paracrine signals from both somatic cell types (granulosa and theca) and from the oocyte. TGF-β superfamily members expressed by follicular cells and implicated in this phase of follicle development include TGF-β, activin, GDF-9/9B and several BMPs. Acquisition of FSH responsiveness is a pre-requisite for growth beyond the small antral stage and evidence indicates an autocrine role for granulosa-derived activin in promoting granulosa cell proliferation, FSH receptor expression and aromatase activity. Indeed, some of the effects of FSH on granulosa cells may be mediated by endogenous activin. At the same time, activin may act on theca cells to attenuate LH-dependent androgen production in small to medium-size antral follicles. Dominant follicle selection appears to depend on differential FSH sensitivity amongst a growing cohort of small antral follicles. Activin may contribute to this selection process by sensitizing those follicles with the highest "activin tone" to FSH. Production of inhibin, like estradiol, increases in selected dominant follicles, in an FSH- and insulin-like growth factor-dependent manner and may exert a paracrine action on theca cells to upregulate LH-induced secretion of androgen, an essential requirement for further estradiol secretion by the pre-ovulatory follicle. Like activin, BMP-4 and -7 (mostly from theca), and BMP-6 (mostly from oocyte), can enhance estradiol and inhibin secretion by bovine granulosa cells while suppressing progesterone secretion; this suggests a functional role in delaying follicle luteinization and/or atresia. Follistatin, may favor luteinization and/or atresia by bio-neutralizing intrafollicular activin and BMPs. Activin receptors are expressed by the oocyte and activin may have a further intrafollicular role in the terminal stages of follicle differentiation to promote oocyte maturation and developmental competence. In a reciprocal manner, oocyte-derived GDF-9/9B may act on the surrounding cumulus granulosa cells to attenuate estradiol output and promote progesterone and hyaluronic acid production, mucification and cumulus expansion.

REFERENCE COUNT: 97 THERE ARE 97 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 18 OF 87 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:436115 CAPLUS
DOCUMENT NUMBER: 139:374393
TITLE: Hyaluronan, a major non-protein glycosaminoglycan component of the extracellular matrix in human bone marrow, mediates dexamethasone resistance in multiple myeloma
AUTHOR(S): Vincent, Thierry; Molina, Laurence; Espert, Lucile; Mechti, Nadir
CORPORATE SOURCE: INSERM Unite U475 and UMR-CNRS5094, Montpellier, Fr.
SOURCE: British Journal of Haematology (2003), 121(2), 259-269
CODEN: BJHEAL; ISSN: 0007-1048
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal

LANGUAGE: English

AB Originating from a post-switch memory B cell or plasma cell compartment in peripheral lymphoid tissues, malignant multiple myeloma (MM) cells accumulate in the bone marrow of patients with MM. In this favorable microenvironment, their growth and survival are dependent upon both soluble factors and phys. cell-to-cell and cell-to-extracellular-matrix contacts. In this study, hyaluronan (HA), a major non-protein glycosaminoglycan component of the extracellular matrix in mammalian bone marrow, acted as a survival factor against dexamethasone (Dex)-induced apoptosis in MM cell lines. These effects were mediated through an interleukin 6 (IL-6) autocrine pathway, involving signal transducers and activators of transcription-3 phosphorylation on IL-6-dependent XG-1 and XG-6 cell lines. HA promoted accumulation of IL-6 in the culture medium without affecting IL-6 gene expression, suggesting that HA protects, stabilizes and concs. IL-6 close to its site of secretion, thus favoring its autocrine activity. In contrast, in the IL-6-independent RPMI8226 cell line, HA survival effect was mediated through a gp80-IL-6 receptor-independent pathway, resulting in the up-regulation of Bcl-2 anti-apoptotic protein expression and nuclear factor-κB activation. Taken together, these data suggest that HA antagonizes Dex-induced apoptosis of MM cells by favoring the autocrine activity of different cytokines or growth factors. As HA is a major component of the bone marrow extracellular matrix, these findings support the idea that HA could play a major role in the survival of MM cells in vivo, and could explain why MM cells accumulate in the bone marrow of patients with MM and escape conventional chemotherapy.

REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 19 OF 87 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:695832 CAPLUS
DOCUMENT NUMBER: 137:222118
TITLE: Grafts for the repair of osteochondral defects
INVENTOR(S): Pavesio, Alessandra; Callegaro, Landranco
PATENT ASSIGNEE(S): Fidia Advanced Biopolymers S.r.l., Italy
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002070030	A1	20020912	WO 2002-EP1224	20020206
WO 2002070030	C1	20021205		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2437440	AA	20020912	CA 2002-2437440	20020206
EP 1357953	A1	20031105	EP 2002-726105	20020206
EP 1357953	B1	20051109		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004524904	T2	20040819	JP 2002-569201	20020206
AT 309007	E	20051115	AT 2002-726105	20020206
ES 2250642	T3	20060416	ES 2002-2726105	20020206

US 2004076656 A1 20040422 US 2003-467142 20030804
PRIORITY APPLN. INFO.: IT 2001-PD32 A 20010209
WO 2002-EP1224 W 20020206

AB The invention concerns the preparation and use of a biocompatible, biocomponent material constituted by: (a) a three-dimensional matrix of hyaluronic acid derivs. with a structure containing empty spaces; (b) a porous, three-dimensional matrix constituted by a ceramic material; (c) possibly containing pharmacol. or biol. active ingredients. Cultured mesenchymal stem cells exposed to β1-transforming growth factors were loaded into a sponge made of a hyaluronan derivative (Hyaff-11) for the construction of the cartilage component of the composite graft. Mesenchymal stem cells exposed to osteogenic supplement were loaded into a porous calcium phosphate ceramic component for bone formation. Cell-loaded Hyaff-11 sponge and ceramic were assembled and joined together with fibrin glue to form a composite osterochondral graft. Said graft was incubated at 37° for 30 min and then grafted s.c. into the backs of syngeneic rats and the animals were sacrificed 6 wk later. After six weeks, well-organized fibrocartilage was distributed through the material that is partially absorbed. The sep. formation of cartilage and bone could be seen in the two material. Neither the bone tissue nor the cartilage crosses the tidemark between the two materials. At the same time, the two materials formed a structurally integrated composite material thanks to the presence of fibrous tissue and collagen fibers that do cross tidemark.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 20 OF 87 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:495934 CAPLUS
DOCUMENT NUMBER: 138:130798
TITLE: Control of capillary formation by membrane-anchored extracellular inhibitor of phospholipase A2
AUTHOR(S): Chen, W. M.; Soria, J.; Soria, C.; Krimsky, M.; Yedgar, S.
CORPORATE SOURCE: INSERM - EMI 99-12, Hotel Dieu, Paris, INSERM -EMI 99-12, Fr.
SOURCE: FEBS Letters (2002), 522(1-3), 113-118
CODEN: FEBLAL; ISSN: 0014-5793
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Secretory phospholipase A2 (sPLA2) has been reported to be involved in cell proliferation in general and in endothelial cell migration, processes required for capillary formation. Subsequently, we examined the potential control of angiogenesis by sPLA2 inhibition, using a cell-impermeable sPLA2 inhibitor composed of N-derivatized phosphatidyl-ethanolamine linked to hyaluronic acid. This inhibitor effectively inhibits the proliferation and migration of human bone marrow endothelial cells in a dose-dependent manner, and suppresses capillary formation induced by growth factors involved in vascularization of tumors and of atherosclerotic plaques. It is proposed that sPLA2 inhibition introduces a novel approach in the control of cancer development and atherosclerosis.

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 21 OF 87 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:269189 CAPLUS
DOCUMENT NUMBER: 136:277384
TITLE: Study on the mechanism of the growth failure in children with juvenile rheumatoid arthritis
AUTHOR(S): Mori, Hirosumi
CORPORATE SOURCE: Department of Pediatrics, Faculty of Medicine,

Kagoshima University, Kagoshima, 890-8520, Japan
SOURCE: Kagoshima Daigaku Igaku Zasshi (2002), 53(4), 67-72
CODEN: KDIZAA; ISSN: 0368-5063
PUBLISHER: Kagoshima Daigaku Igakkai
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
AB Growth failure is a feature of juvenile rheumatoid arthritis (JRA), but its mechanism has not been clearly explained. A total of 23 JRA children were examined for their annual growth rate with several factors relating to the growth and bone metabolism Growth impairment was observed only in active stage of systemic and polyarticular JRA. In these patients, the growth rate significantly correlated with levels of insulin-like growth factor-1, osteocalcin, hyaluronic acid, and pyridinoline. As these markers are known to correlate with inflammatory cytokines, it is suggested that the inflammatory cytokines may play an essential role in the development of growth retardation in JRA.

L18 ANSWER 22 OF 87 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:246096 CAPLUS
DOCUMENT NUMBER: 137:268360
TITLE: Evaluation of a collagen-hyaluronate bilayer matrix for bone and cartilage repair
AUTHOR(S): Liu, Lin-Shu; Thompson, Andrea; Daverman, Robin; Poser, James W.; Spiro, Robert C.
CORPORATE SOURCE: Orquest, Inc., Mountain View, CA, 94043, USA
SOURCE: Materials Research Society Symposium Proceedings (2001), 662(Biomaterials for Drug Delivery and Tissue Engineering), LL1.9/1-LL1.9/6
CODEN: MRSPDH; ISSN: 0272-9172
PUBLISHER: Materials Research Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We have developed a novel bilayer matrix composed of a porous type I collagen layer that transitions into a hyaluronate gel layer. This study evaluates the potential of the bilayer matrix to support the in vitro and in vivo formation of both bone and cartilage tissue. In the presence of recombinant human growth and differentiation factor-5, fetal rat calvarial cells cultured in the HA layer grew in a round, aggregated, chondrocyte-like morphol., while those in the collagen layer grew flattened and spread. Biochem. anal. demonstrated that cells in the collagen layer expressed higher levels of alkaline phosphatase activity, and lower levels of sulfated glycosaminoglycans and type II collagen when compared to cells in the HA layer. I.m. implants of the bilayer matrix with growth factor retrieved at 28 days revealed the presence of bone and cartilage tissue in the collagen and hyaluronate layers, resp. These results demonstrate that the differentiation of cells in response to a single growth factor can be guided by specific compositional changes of the extracellular matrix.
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 23 OF 87 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:147379 CAPLUS
DOCUMENT NUMBER: 136:205483
TITLE: Viscoelastic and fluid bone filling compositions, applicator packed with them, and the kit
INVENTOR(S): Tanaka, Takaaki; Sazono, Masaaki; Fujii, Katsuyuki; Hamai, Akio
PATENT ASSIGNEE(S): Seikagaku Kogyo Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 7 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent

LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2002058736	A2	20020226	JP 2000-247841	20000817

PRIORITY APPLN. INFO.: JP 2000-247841 20000817

AB The compns. contain (a) 2.0-5.5% (weight/weight) aqueous solution of hyaluronic acid or its pharmacol. acceptable salts having viscosity at 25° ≥110 Pa·s, (b) bone filling materials which are insol. in the solution, and optionally (c) osteogenesis promoting substances, e.g. PTH, calcitonin, vitamin D, IGF, PDGF, etc. Also claimed are applicators such as syringes packed with the compns. and bone filling kits containing (a), (b), and optionally the applicator. Bone defects are simply and closely filled with the compns.

L18 ANSWER 24 OF 87 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:861937 CAPLUS
DOCUMENT NUMBER: 137:145461
TITLE: Osteogenesis of large segmental radius defects enhanced by basic fibroblast growth factor activated bone marrow stromal cells grown on non-woven hyaluronic acid-based polymer scaffold
AUTHOR(S): Lisignoli, G.; Fini, M.; Giavaresi, G.; Nicoli Aldini, N.; Toneguzzi, S.; Facchini, A.
CORPORATE SOURCE: Laboratorio di Immunologia e Genetica, Istituti Ortopedici Rizzoli, Bologna, 40136, Italy
SOURCE: Biomaterials (2001), Volume Date 2002, 23(4), 1043-1051
CODEN: BIMADU; ISSN: 0142-9612
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Osteogenesis of large segmental radius defects in a rat model was studied by implanting a biodegradable non-woven hyaluronic acid-based polymer scaffold (Hyaff 11) alone or in combination with bone marrow stromal cells (BMSCs). These cells had been previously grown in vitro in mineralizing medium either supplemented with basic fibroblast growth factor (bFGF) or unsupplemented. The healing of bone defects was evaluated at 40, 80, 160 and 200 days and the repair process investigated by radiog., histomorphometric (assessment of new bone growth and lamellar bone) and histol. analyses (toluidine blue and von Kossa staining). Mineralization of bone defects occurred in the presence of the Hyaff 11 scaffold alone or when combined with BMSCs grown with or without bFGF, but each process had a different timing. In particular, bFGF significantly induced mineralization from day 40, whereas 160 days were necessary for direct evidence that a similar process was developing under the other two conditions tested (scaffold alone or with BMSCs).Radiog. score, new bone growth and lamellar bone percentage were highly correlated. The present outcomes were further confirmed by toluidine blue and von Kossa staining. According to these in vivo findings, the Hyaff 11 scaffold is an appropriate carrier vehicle for the repair of bone defects; addnl., it can significantly accelerate bone mineralization in combination with BMSCs and bFGF.

REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 25 OF 87 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:662793 CAPLUS
DOCUMENT NUMBER: 136:374747

TITLE: Tissue-engineered fabrication of an osteochondral composite graft using rat bone marrow-derived mesenchymal stem cells
AUTHOR(S): Gao, Jizong; Dennis, James E.; Solchaga, Luis A.; Awadallah, Amad S.; Goldberg, Victor M.; Caplan, Arnold I.
CORPORATE SOURCE: Skeletal Research Center, Case Western Reserve University, Cleveland, OH, USA
SOURCE: Tissue Engineering (2001), 7(4), 363-371
CODEN: TIENFP; ISSN: 1076-3279
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB This study tested the tissue engineering hypothesis that construction of an osteochondral composite graft could be accomplished using multipotent progenitor cells and phenotype-specific biomaterials. Rat bone marrow-derived mesenchymal stem cells (MSCs) were culture-expanded and sep. stimulated with transforming growth factor -β1 (TGF-β1) for chondrogenic differentiation or with an osteogenic supplement (OS). MSCs exposed to TGF-β1 were loaded into a sponge composed of a hyaluronan derivative (HYAFF-11) for the construction of the cartilage component of the composite graft, and MSCs exposed to OS were loaded into a porous calcium phosphate ceramic component for bone formation. Cell-loaded HYAFF-11 sponge and ceramic were joined together with fibrin sealant, Tisseel, to form a composite osteochondral graft, which was then implanted into a s.c. pocket in syngeneic rats. Specimens were harvested at 3 and 6 wk after implantation, examined with histol. for morphol. features, and stained immunohistochem. for type I, II, and X collagen. The two-component composite graft remained as an integrated unit after in vivo implantation and histol. processing. Fibrocartilage was observed in the sponge, and bone was detected in the ceramic component. Observations with polarized light indicated continuity of collagen fibers between the ceramic and HYAFF-11 components in the 6-wk specimens. Type I collagen was identified in the neo-tissue in both sponge and ceramic, and type II collagen in the fibrocartilage, especially the pericellular matrix of cells in the sponge. These data suggest that the construction of a tissue-engineered composite osteochondral graft is possible with MSCs and different biomaterials and bioactive factors that support either chondrogenic or osteogenic differentiation.

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 26 OF 87 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:526558 CAPLUS
DOCUMENT NUMBER: 135:322670
TITLE: Basic fibroblast growth factor enhances in vitro mineralization of rat bone marrow stromal cells grown on nonwoven hyaluronic acid based polymer scaffold
AUTHOR(S): Lisignoli, G.; Zini, N.; Remiddi, G.; Piacentini, A.; Puggioli, A.; Trimarchi, C.; Fini, M.; Maraldi, N. M.; Facchini, A.
CORPORATE SOURCE: Laboratorio di Immunologia e Genetica, Istituti Ortopedici Rizzoli, Bologna, 40136, Italy
SOURCE: Biomaterials (2001), 22(15), 2095-2105
CODEN: BIMADU; ISSN: 0142-9612
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A biodegradable nonwoven hyaluronic acid polymer scaffold (Hyaff 11) was analyzed in vitro as a carrier vehicle for differentiation and mineralization of rat bone marrow stromal cells (BMSC). BMSC were grown on Hyaff 11 in a mineralizing medium in the presence/absence of

basic fibroblast growth factor (bFGF). Osteoblastic differentiation was investigated by light and electron microscopy analyzing the expression of osteogenic markers: calcium, alkaline phosphatase (AP), osteopontin (OP), bone sialoprotein (BSP) and collagen type I. The authors also measured proliferation, AP activity and mRNA expression of AP and osteocalcin (OC). Electron microscopy and Toluidine-blue staining demonstrated that bFGF accelerated (day 20 vs. day 40) and increased mineralization. With bFGF, calcium, OP and BSP were strongly enhanced at day 40, whereas AP decreased. Our in vitro results demonstrate that Hyaff 11 is a useful vehicle for growth, differentiation and mineralization of rat BMSC, and that it permits bone development.

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:528534 CAPLUS
DOCUMENT NUMBER: 140:187234
TITLE: Repair of reconstituted freeze-dried bone allograft to segmental radius defects in rabbits
AUTHOR(S): Chen, Qing; Gu, Jiefu; Cai, Lin; Gan, Yu
CORPORATE SOURCE: Zhongnan Hospital, Wuhan University, Wuhan, 430071, Peop. Rep. China
SOURCE: Wuhan Daxue Xuebao, Yixueban (2002), 23(3), 251-254
CODEN: WDXYAA
PUBLISHER: Wuhan Daxue Xuebao, Yixueban Faxingbu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB The effect of basic fibroblast growth factor (bFGF) and hyaluronic acid gel (HAG) combined with freeze-dried bone allograft in repairing radius defects was investigated and their mechanism was explored. Fifteen mm segmental bone/periosteum defects were created in 36 New Zealand rabbits on bilateral radius and were treated with three different kinds of implants: A, bFGF and HAG combined with freeze-dried bone; B, bFGF combined with freeze-dried bone; C, a single freeze-dried bone as control. The repairs of defects were observed by radiol. and histol. method and analyzed by radionuclide bone imaging, and calcium contents were detected at different periods. The new bone formation, bone metabolic activity and calcium contents of defects in Group A were higher than that in Group B, and the data of Group B were higher than that in Group C. The defects of Group A were healed at the 8th week, and those of Group B were healed at the 10th week. As an osteogenetic factor, bFGF promotes the new bone formation. As a slow-release carrier, HAG enhances the effectiveness of bFGF. The combination of bFGF, HAG and freeze-dried bone allograft can repair the defects more effectively.

L19 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:29537 CAPLUS
DOCUMENT NUMBER: 138:78545
TITLE: Hyaluronic acid gel-based cell culture substrates for tissue regeneration
INVENTOR(S): Kato, Yukio; Tsutsumi, Shinichi; Miyazaki, Kazuko; Hara, Maiko; Kawaguchi, Hiroyuki; Kurihara, Hidemi; Miyoshi, Shozo; Hashimoto, Masamichi; Himeta, Koichi
PATENT ASSIGNEE(S): Denki Kagaku Kogyo Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 8 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2003010308	A2	20030114	JP 2001-196687	20010628
PRIORITY APPLN. INFO.:			JP 2001-196687	20010628

AB The substrate is made of hyaluronic acid (I) gel which is not substantially modified with chemical crosslinking agents or chemical modifying agents and is slightly-soluble in neutral aqueous solution Animal cells, e.g. chondrocytes, stem cells, bone marrow cells, osteoblasts, ES cells, etc., are disseminated on the substrate and the substrate containing the surviving cells is applied to defective parts of tissues to regenerate tissues, e.g. articular cartilage, costal cartilage, tracheal cartilage, skull, periodontium, cementum tendon, ligament, etc. The gel may be in the forms of sheets, films, sponges, fibers, tubes, etc., and contain

bioactive substances such as cell growth factors, antibiotics, proteins, oligosaccharides, or nucleic acids. I with mol. weight 2 + 106 dalton was dissolved in H2O and the solution was adjusted to pH 1.5 with HNO3 and frozen in a flat-bottomed container at -20° for 5 days. The frozen product was soaked in a phosphate-buffered saline solution for 24 h and dried to give sponge-like gel. Rabbit femur- and tibia-derived mesenchymal cells (preparation given) were disseminated on the gel and incubated to become confluent in the presence of bFGF. Subculture was repeated twice and the 3rd subculture was implanted into a drilled hole formed in knee articular cartilage of a rabbit to promote regeneration of cartilage and bone.

L19 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:861937 CAPLUS
DOCUMENT NUMBER: 137:145461
TITLE: Osteogenesis of large segmental radius defects enhanced by basic fibroblast growth factor activated bone marrow stromal cells grown on non-woven hyaluronic acid-based polymer scaffold
AUTHOR(S): Lisignoli, G.; Fini, M.; Giavaresi, G.; Nicoli Aldini, N.; Toneguzzi, S.; Facchini, A.
CORPORATE SOURCE: Laboratorio di Immunologia e Genetica, Istituti Ortopedici Rizzoli, Bologna, 40136, Italy
SOURCE: Biomaterials (2001), Volume Date 2002, 23(4), 1043-1051
CODEN: BIMADU; ISSN: 0142-9612
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Osteogenesis of large segmental radius defects in a rat model was studied by implanting a biodegradable non-woven hyaluronic acid-based polymer scaffold (Hyaff 11) alone or in combination with bone marrow stromal cells (BMSCs). These cells had been previously grown in vitro in mineralizing medium either supplemented with basic fibroblast growth factor (bFGF) or unsupplemented. The healing of bone defects was evaluated at 40, 80, 160 and 200 days and the repair process investigated by radiog., histomorphometric (assessment of new bone growth and lamellar bone) and histol. analyses (toluidine blue and von Kossa staining). Mineralization of bone defects occurred in the presence of the Hyaff 11 scaffold alone or when combined with BMSCs grown with or without bFGF, but each process had a different timing. In particular, bFGF significantly induced mineralization from day 40, whereas 160 days were necessary for direct evidence that a similar process was developing under the other two conditions tested (scaffold alone or with BMSCs).Radiog. score, new bone growth and lamellar bone percentage were highly correlated. The present outcomes were further confirmed by toluidine blue and von Kossa staining. According to these in vivo findings, the Hyaff 11 scaffold is an appropriate carrier vehicle for the repair of bone defects; addnl., it can significantly accelerate bone mineralization in combination with BMSCs and bFGF.
REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:526558 CAPLUS
DOCUMENT NUMBER: 135:322670
TITLE: Basic fibroblast growth factor enhances in vitro mineralization of rat bone marrow stromal cells grown on nonwoven hyaluronic acid based polymer scaffold
AUTHOR(S): Lisignoli, G.; Zini, N.; Remiddi, G.; Piacentini, A.; Puggioli, A.; Trimarchi, C.; Fini, M.; Maraldi, N. M.; Facchini, A.

CORPORATE SOURCE: Laboratorio di Immunologia e Genetica, Istituti Ortopedici Rizzoli, Bologna, 40136, Italy
SOURCE: Biomaterials (2001), 22(15), 2095-2105
CODEN: BIMADU; ISSN: 0142-9612
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A biodegradable nonwoven hyaluronic acid polymer scaffold (Hyaff 11) was analyzed in vitro as a carrier vehicle for differentiation and mineralization of rat bone marrow stromal cells (BMSC). BMSC were grown on Hyaff 11 in a mineralizing medium in the presence/absence of basic fibroblast growth factor (bFGF). Osteoblastic differentiation was investigated by light and electron microscopy analyzing the expression of osteogenic markers: calcium, alkaline phosphatase (AP), osteopontin (OP), bone sialoprotein (BSP) and collagen type I. The authors also measured proliferation, AP activity and mRNA expression of AP and osteocalcin (OC). Electron microscopy and Toluidine-blue staining demonstrated that bFGF accelerated (day 20 vs. day 40) and increased mineralization. With bFGF, calcium, OP and BSP were strongly enhanced at day 40, whereas AP decreased. Our in vitro results demonstrate that Hyaff 11 is a useful vehicle for growth, differentiation and mineralization of rat BMSC, and that it permits bone development.

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:294955 CAPLUS
DOCUMENT NUMBER: 134:290753
TITLE: Method of promoting bone growth with hyaluronic acid and growth factors
INVENTOR(S): Radomsky, Michael
PATENT ASSIGNEE(S): Orquest, Inc., USA
SOURCE: U.S., 11 pp., Cont.-in-part of U.S. 5,942,499.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6221854	B1	20010424	US 1999-360543	19990726
US 5942499	A	19990824	US 1997-811971	19970305
CA 2378328	AA	20010201	CA 2000-2378328	20000726
WO 2001007056	A1	20010201	WO 2000-US20373	20000726
WO 2001007056	C2	20020725		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1198235	A1	20020424	EP 2000-950736	20000726
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003505422	T2	20030212	JP 2001-511940	20000726
NZ 516097	A	20040227	NZ 2000-516097	20000726
AU 777328	B2	20041014	AU 2000-63797	20000726
US 2001014664	A1	20010816	US 2001-825688	20010403
US 6703377	B2	20040309		

US 2004176295	A1	20040909	US 2004-796441		20040308
AU 2005200146	A1	20050210	AU 2005-200146		20050113
PRIORITY APPLN. INFO.:			US 1996-611690	B2	19960305
			US 1997-811971	A2	19970305
			US 1999-360543	A	19990726
			WO 2000-US20373	W	20000726
			US 2001-825688	A1	20010403

AB A bone growth-promoting composition is provided comprising hyaluronic acid and a growth factor. The composition has a viscosity and biodegradability sufficient to persist at an intra-articular site of desired bone growth for a period of time sufficient to promote the bone growth. Preferably hyaluronic acid is used in a composition range of 0.1-4% by weight and preferred growth factor is bFGF, present in a concentration range of about 10#-6 to 100 mg/mL.

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:78247 CAPLUS
DOCUMENT NUMBER: 134:125970
TITLE: Method of promoting bone growth with hyaluronic acid and growth factors
INVENTOR(S): Randomsky, Michael
PATENT ASSIGNEE(S): Orquest, Inc., USA
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001007056	A1	20010201	WO 2000-US20373	20000726
WO 2001007056	C2	20020725		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6221854	B1	20010424	US 1999-360543	19990726
CA 2378328	AA	20010201	CA 2000-2378328	20000726
EP 1198235	A1	20020424	EP 2000-950736	20000726
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003505422	T2	20030212	JP 2001-511940	20000726
NZ 516097	A	20040227	NZ 2000-516097	20000726
AU 777328	B2	20041014	AU 2000-63797	20000726
AU 2005200146	A1	20050210	AU 2005-200146	20050113

PRIORITY APPLN. INFO.:		US 1999-360543	A	19990726
		US 1996-611690	B2	19960305
		US 1997-811971	A2	19970305
		WO 2000-US20373	W	20000726

AB A bone growth-promoting composition is provided comprising hyaluronic acid and a growth factor. The composition has a viscosity and biodegradability sufficient to persist at an intra-articular site of desired bone growth for a period of time sufficient to promote the bone growth. Preferably hyaluronic acid is used in a composition range of 0.1-4 % by weight and

preferred growth factor is bFGF, present in a concentration range of about 10-6 to 100 mg/mL.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:537943 CAPLUS
DOCUMENT NUMBER: 131:161648
TITLE: Method of promoting bone growth with hyaluronic acid and growth factors
INVENTOR(S): Radomsky, Michael
PATENT ASSIGNEE(S): Orquest, Inc., USA
SOURCE: U.S., 12 pp., Cont.-in-part of U. S. Ser. No.611,690, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5942499	A	19990824	US 1997-811971	19970305
CN 1212628	A	19990331	CN 1997-192822	19970305
NZ 331238	A	20000526	NZ 1997-331238	19970305
US 6645945	B1	20031111	US 1999-298539	19990422
US 6221854	B1	20010424	US 1999-360543	19990726
US 2001014664	A1	20010816	US 2001-825688	20010403
US 6703377	B2	20040309		
US 2004176295	A1	20040909	US 2004-796441	20040308

PRIORITY APPLN. INFO.:
US 1996-611690 B2 19960305
US 1997-811971 A 19970305
WO 1997-US4810 W 19970305
US 1999-360543 A3 19990726
US 2001-825688 A1 20010403

AB A bone growth-promoting composition is provided comprising hyaluronic acid and a growth factor. The composition has a viscosity and biodegradability sufficient to persist at the site of desired bone growth for a period of time sufficient to promote the bone growth. Preferably hyaluronic acid is used in a composition range of 0.1-4 % and preferred growth factor is bFGF, present in a concentration range of about 10-6 to 100 mg/mL.

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:617981 CAPLUS
DOCUMENT NUMBER: 127:253211
TITLE: Method of promoting bone growth with hyaluronic acid and growth factors
INVENTOR(S): Radomsky, Michael
PATENT ASSIGNEE(S): Orquest, Inc., USA
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9732591	A1	19970912	WO 1997-US4810	19970305

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,

DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, YU
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

CA 2246747	AA	19970912	CA 1997-2246747		19970305
AU 9725449	A1	19970922	AU 1997-25449		19970305
AU 729086	B2	20010125			
CN 1212628	A	19990331	CN 1997-192822		19970305
EP 910389	A1	19990428	EP 1997-916976		19970305
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
NZ 331238	A	20000526	NZ 1997-331238		19970305
JP 2002504083	T2	20020205	JP 1997-532070		19970305
PRIORITY APPLN. INFO.:			US 1996-611690	A	19960305
			US 1997-811971	A	19970305
			WO 1997-US4810	W	19970305

AB A bone growth-promoting composition is provided comprising hyaluronic acid and a growth factor. The composition has a viscosity and biodegradability sufficient to persist at the site of desired bone growth for a period of time sufficient to promote the bone growth. Preferably hyaluronic acid is used in a composition range of 0.1 to 4 % and preferred growth factor is bFGF, present in a concentration range of 10-6 to 100 mg/mL. An aqueous solution containing Na hyaluronate, bFGF, and Na citrate was injected with a needle between the periosteum and parietal bone of rats. The animals were euthanized 14 days following treatment and new bone formation was evaluated.

L19 ANSWER 9 OF 12 MEDLINE on STN

ACCESSION NUMBER:	2003381100 MEDLINE
DOCUMENT NUMBER:	PubMed ID: 12916297
TITLE:	Experimental study of repairing segmental bone defect with reconstituted freeze-dried bone allograft.
AUTHOR:	Chen Qing; Gu Jie-fu; Cai Lin
CORPORATE SOURCE:	Department of Orthopedic Surgery, Central Hospital of Wuhan, Wuhan, Hubei, P. R. China 430014.
SOURCE:	Zhongguo xiu fu chong jian wai ke za zhi = Zhongguo xiufu chongjian waike zazhi = Chinese journal of reparative and reconstructive surgery, (2003 Jan) Vol. 17, No. 1, pp. 5-8. Journal code: 9425194. ISSN: 1002-1892.
PUB. COUNTRY:	China
DOCUMENT TYPE:	Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:	Chinese
FILE SEGMENT:	Priority Journals
ENTRY MONTH:	200312
ENTRY DATE:	Entered STN: 15 Aug 2003 Last Updated on STN: 18 Dec 2003 Entered Medline: 17 Dec 2003

AB OBJECTIVE: To study the effect of basic fibroblast growth factor (bFGF) and hyaluronic acid gel (HAG) combined with freeze-dried bone allograft in repairing segmental bone defect and to explore their mechanism. METHODS: The 15 mm segmental bone/periosteum defects were created on bilateral radius in 50 New Zealand rabbits and were treated with four different kinds of implants on 25 radius respectively (group A: bFGF and HAG combined with freeze-dried bone; group B: bFGF combined with freeze-dried bone; group C: HAG combined with freeze-dried bone; group D: simple freeze-dried bone as a control). The repair of defect was observed radiologically and histologically and were analyzed by radionuclide bone imaging and measurement of calcium contents at different periods. RESULTS: The new bone formation, bone metabolic activity and

calcium contents of defects were higher in group A than in group B (P < 0.05), and were higher in group B than in groups C and D (P < 0.05). There were no significant difference between groups C and D. The bone defects healed in the 8th week in group A, in the 10th week in group B, but did not healed in the 10th week in groups C and D. CONCLUSION: As an osteogenetic factor, bFGF promotes the new bone formation; as a slow-release carrier, HAG enhances the effectiveness of bFGF. The combination of bFGF, HAG and freeze-dried bone allograft can repair the segmental bone defect more effectively.

L19 ANSWER 10 OF 12 MEDLINE on STN
ACCESSION NUMBER: 2002066655 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11791907
TITLE: Osteogenesis of large segmental radius defects enhanced by basic fibroblast growth factor activated bone marrow stromal cells grown on non-woven hyaluronic acid-based polymer scaffold.
AUTHOR: Lisignoli G; Fini M; Giavaresi G; Nicoli Aldini N; Toneguzzi S; Facchini A
CORPORATE SOURCE: Laboratorio di Immunologia e Genetica, Istituti Ortopedici Rizzoli, Bologna, Italy.
SOURCE: Biomaterials, (2002 Feb) Vol. 23, No. 4, pp. 1043-51. Journal code: 8100316. ISSN: 0142-9612.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200207
ENTRY DATE: Entered STN: 25 Jan 2002
Last Updated on STN: 25 Jul 2002
Entered Medline: 24 Jul 2002
AB Osteogenesis of large segmental radius defects in a rat model was studied by implanting a biodegradable non-woven hyaluronic acid-based polymer scaffold (Hyaff 11) alone or in combination with bone marrow stromal cells (BMSCs). These cells had been previously grown in vitro in mineralising medium either supplemented with basic fibroblast growth factor (bFGF) or unsupplemented. The healing of bone defects was evaluated at 40, 80, 160 and 200 days and the repair process investigated by radiographic, histomorphometric (assessment of new bone growth and lamellar bone) and histological analyses (toluidine blue and von Kossa staining). Mineralisation of bone defects occurred in the presence of the Hyaff 11 scaffold alone or when combined with BMSCs grown with or without bFGF, but each process had a different timing. In particular, bFGF significantly induced mineralisation from day 40, whereas 160 days were necessary for direct evidence that a similar process was developing under the other two conditions tested (scaffold alone or with BMSCs). Radiographic score, new bone growth and lamellar bone percentage were highly correlated. The present outcomes were further confirmed by toluidine blue and von Kossa staining. According to these in vivo findings, the Hyaff 11 scaffold is an appropriate carrier vehicle for the repair of bone defects; additionally, it can significantly accelerate bone mineralisation in combination with BMSCs and bFGF.

L19 ANSWER 11 OF 12 MEDLINE on STN
ACCESSION NUMBER: 2002016690 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11432589
TITLE: Basic fibroblast growth factor enhances in vitro mineralization of rat bone marrow stromal cells grown on non-woven hyaluronic acid based polymer scaffold.
AUTHOR: Lisignoli G; Zini N; Remiddi G; Piacentini A; Puggioli A; Trimarchi C; Fini M; Maraldi N M; Facchini A

CORPORATE SOURCE: Laboratorio di Immunologia e Genetica. Istituti Ortopedici Rizzoli, Bologna, Italy.
SOURCE: Biomaterials, (2001 Aug) Vol. 22, No. 15, pp. 2095-105. Journal code: 8100316. ISSN: 0142-9612.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 21 Jan 2002
Last Updated on STN: 21 Jan 2002
Entered Medline: 7 Dec 2001

AB A biodegradable non-woven hyaluronic acid polymer scaffold (Hyaff 11) was analysed in vitro as a carrier vehicle for differentiation and mineralization of rat bone marrow stromal cells (BMSC). BMSC were grown on Hyaff 11 in a mineralizing medium in the presence/absence of basic fibroblast growth factor (bFGF). Osteoblastic differentiation was investigated by light and electron microscopy analysing the expression of osteogenic markers: calcium, alkaline phosphatase (AP), osteopontin (OP), bone sialoprotein (BSP) and collagen type 1. We also measured proliferation, AP activity and mRNA expression of AP and osteocalcin (OC). Electron microscopy and Toluidine-blue staining demonstrated that bFGF accelerated (day 20 vs. day 40) and increased mineralization. With bFGF, calcium, OP and BSP were strongly enhanced at day 40, whereas AP decreased. Our in vitro results demonstrate that Hyaff 11 is a useful vehicle for growth, differentiation and mineralization of rat BMSC, and that it permits bone development.

L19 ANSWER 12 OF 12 MEDLINE on STN
ACCESSION NUMBER: 96212618 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8629452
TITLE: Basic fibroblast growth factor for stimulation of bone formation in osteoinductive or conductive implants.
AUTHOR: Wang J S
CORPORATE SOURCE: Department of Orthopedics, University of Lund, Sweden.
SOURCE: Acta orthopaedica Scandinavica. Supplementum, (1996 Apr) Vol. 269, pp. 1-33. Ref: 204
Journal code: 0370353. ISSN: 0300-8827.
PUB. COUNTRY: Denmark
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199606
ENTRY DATE: Entered STN: 8 Jul 1996
Last Updated on STN: 8 Jul 1996
Entered Medline: 21 Jun 1996

AB Basic Fibroblast Growth Factor (bFGF) is one of the endogenous factors found in bone matrix. bFGF is a mitogen for many cell types, including osteoblasts and chondrocytes. It can stimulate angiogenesis and osteoblast gene expression. The purpose of this study was to investigate whether exogenous bFGF can stimulate the formation of bone in bone grafts and in a bone graft substitute. In a model using demineralized bone matrix implants for bone induction, a dose of 15 ng bFGF per implant increased the number of chondrocytes and the amount of bone, whereas 1900 ng greatly inhibited cartilage and bone formation. These results are consistent with previous studies with this model, showing that a lower dose of bFGF increased bone calcium content and a higher dose reduced it. Thus, exogenous bFGF can stimulate proliferation during early phases of bone induction. A new device, the bone conduction chamber, was developed for the application of bFGF to

bone conductive materials. This model made it possible to demonstrate a difference between the conductive properties of bone grafts and porous hydroxyapatite. bFGF increased bone ingrowth into bone graft inside the chamber and showed a biphasic dose-response curve, so that 8-200 ng per implant (0.4-10 ng/mm3) increased bone ingrowth, but higher or lower doses had no effect. The same doses had the same effects in porous hydroxyapatite. In both bone grafts and porous hydroxyapatite, the highest dose still caused an increase in ingrowth of fibrous tissue. The effect on bone ingrowth was first detected after 6 weeks, regardless if administration of bFGF started at implantation or 2 weeks later, using an implanted minipump. Hyaluronate gel was effective as a slow-release carrier for bFGF. In conclusion, bFGF stimulates bone formation in bone implants, depending on dose and method for administration.

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     (FILE 'HOME' ENTERED AT 17:10:18 ON 06 JUL 2006)

     FILE 'CAPLUS, MEDLINE' ENTERED AT 17:10:29 ON 06 JUL 2006
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L2           132 S HYALURON? (P) GROWTH FACTOR? (P) BONE?
L3            29 S HYALURON? (P) GROWTH FACTOR? (P) BONE? (P) TREAT?
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L8             5 S HYALURON? (P) GROWTH FACTOR? (P) BONE? (P) SYNERGIS?
L9             5 S HYALURON? (P) GROWTH FACTOR? (P) BONE? (P) SYNERG?
L10           12 S HYALURON? (P) GROWTH FACTOR? (P) BONE? (P) APPL?
L11          103 S L2 NOT L3
L12          103 S L11 NOT L5
L13           99 S L11 NOT L8
L14          102 S L11 NOT L7
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L16           98 S L15 NOT L9
L17            0 S L16 NOT L12
L18           87 S L16 NOT L10
L19           12 S HYALURON? (P) GROWTH FACTOR? (P) BONE? (P) BFGF
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